Supporting information

Constituents of Two *Dioscorea* Species that Potentiate Antibiotic Activity against MRSA

Gugu F. Sibandze,[†,§] Paul Stapleton,[†] and Simon Gibbons[,†,‡]*

[†] Research Department of Pharmaceutical and Biological Chemistry, UCL School of Pharmacy, University College London, 29-39 Brunswick Square London, WC1N 1AX.

[§] Eswatini Institute for Research in Traditional Medicine, Medicinal and Indigenous Food Plants, University of Eswatini, Private Bag 4, Kwaluseni, Eswatini, M201

* Email: s.gibbons@uea.ac.uk

Contents

List of Tables

List of Figures

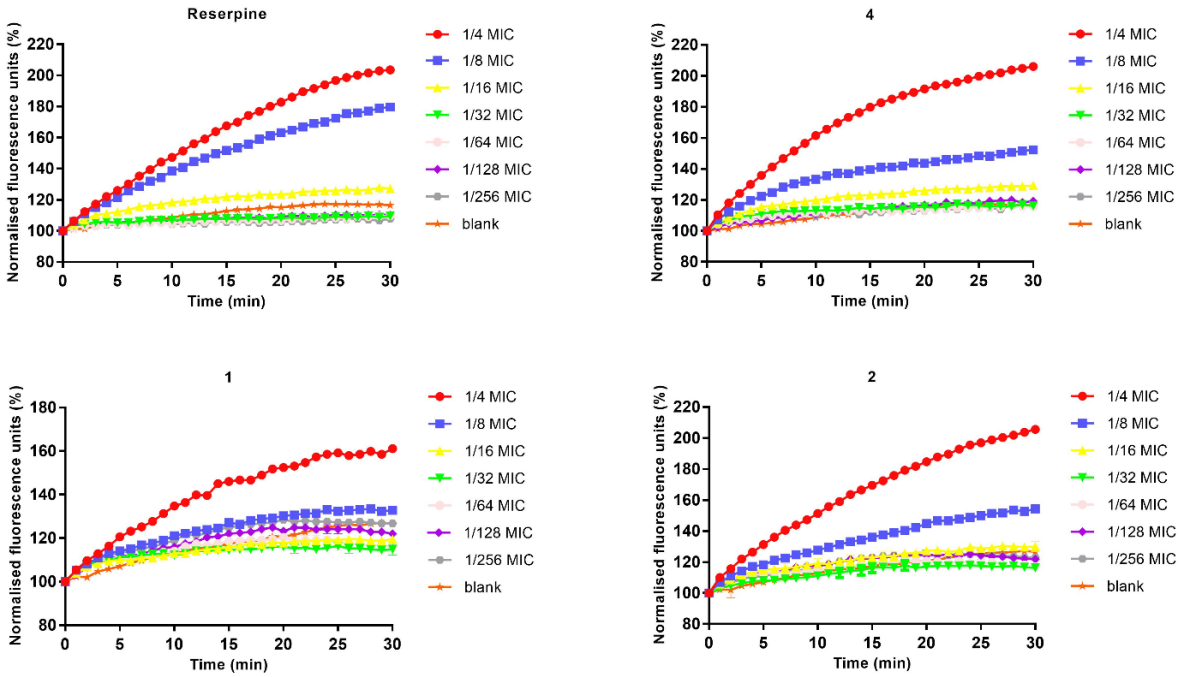

Figure S1: Accumulation of EtBr by *S. aureus* SA-1199B in the Presence of Increasing Concentrations of, from Left to Right; Reserpine, **4**, **1** and **2**.

Table **S**1: Effect of the Compounds on the Intracellular Accumulation of Ethidium Bromide in the *S. aureus* 1199B strain

compound (1/4 MIC)	*S. aureus* 1199B (NorA)	
	Δ slope	RFF (RFF = $RF_{treated} - RF_{untreated}$)[b]
1	1.04	34.45
2	2.45	78.89
4	2.68	89.60
reserpine	2.88	87.08

[b] [where RFtreated is the relative fluorescence of the treated sample and RFuntreated is the relative fluorescence of the blank

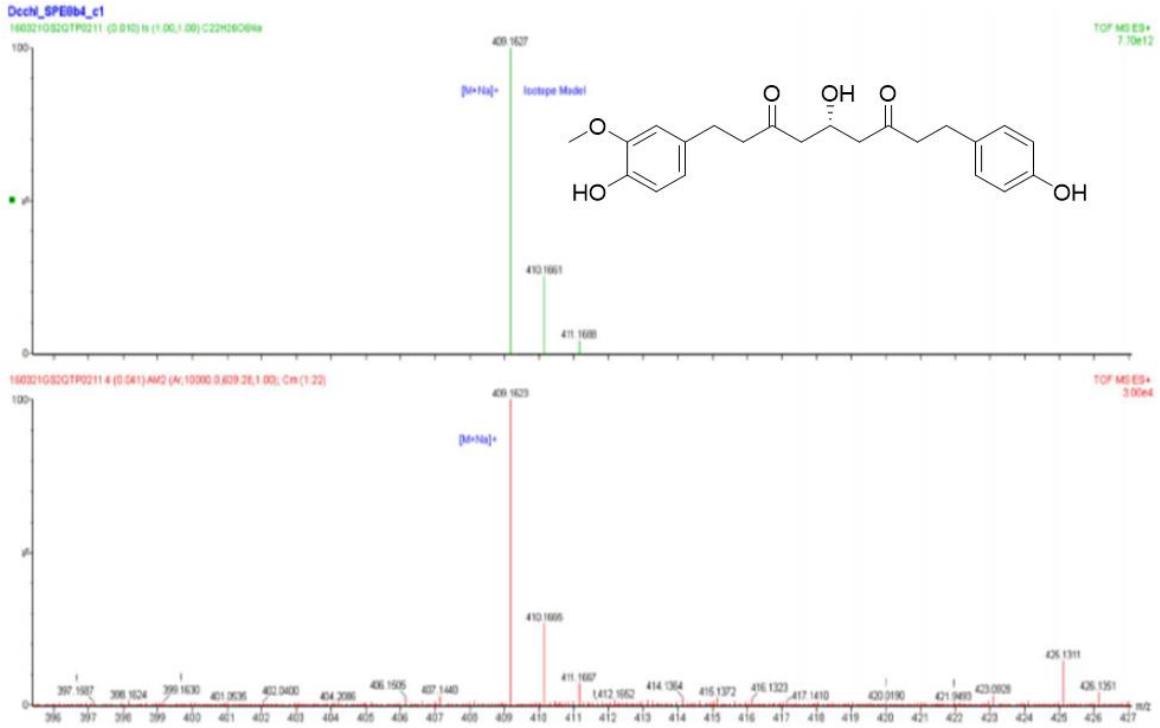

Figure S2: HR-ESI-MS spectrum of **1** in positive ion mode.

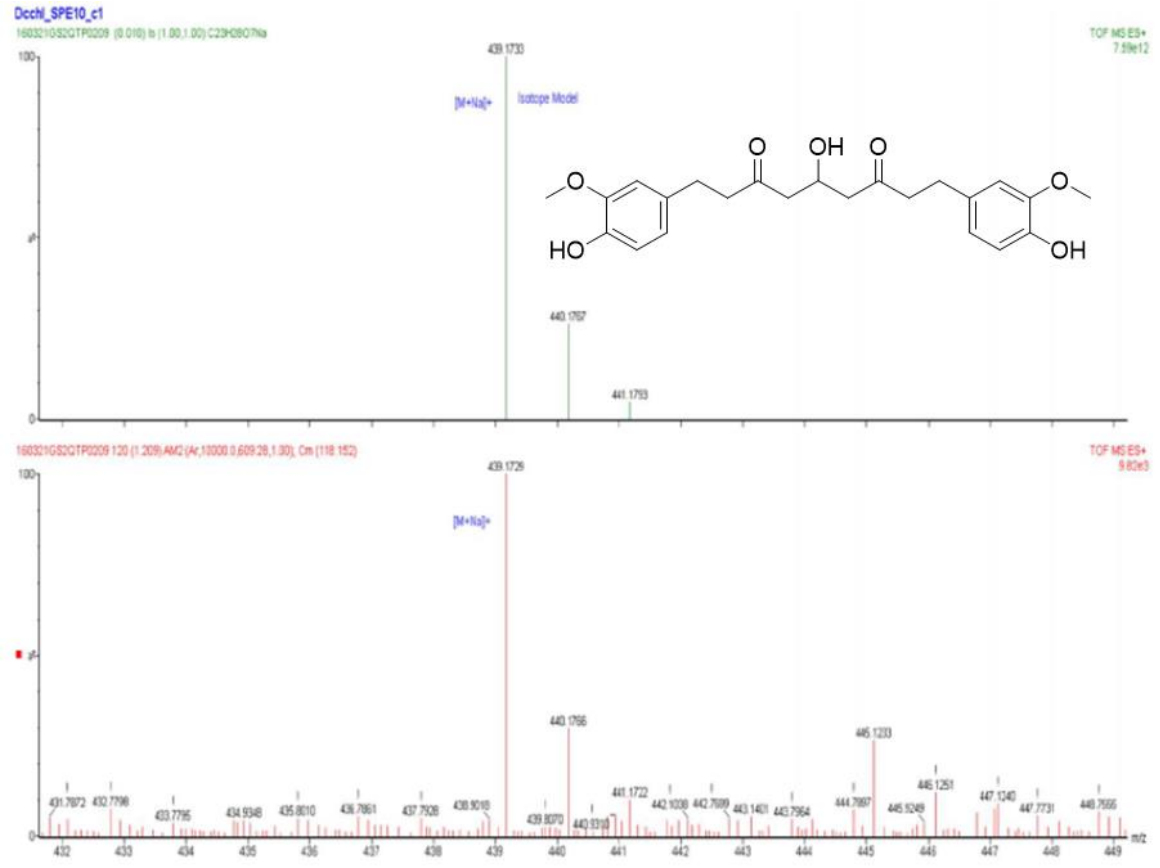

Figure S3: HR-ESI-MS spectrum of **2** in positive ion mode.

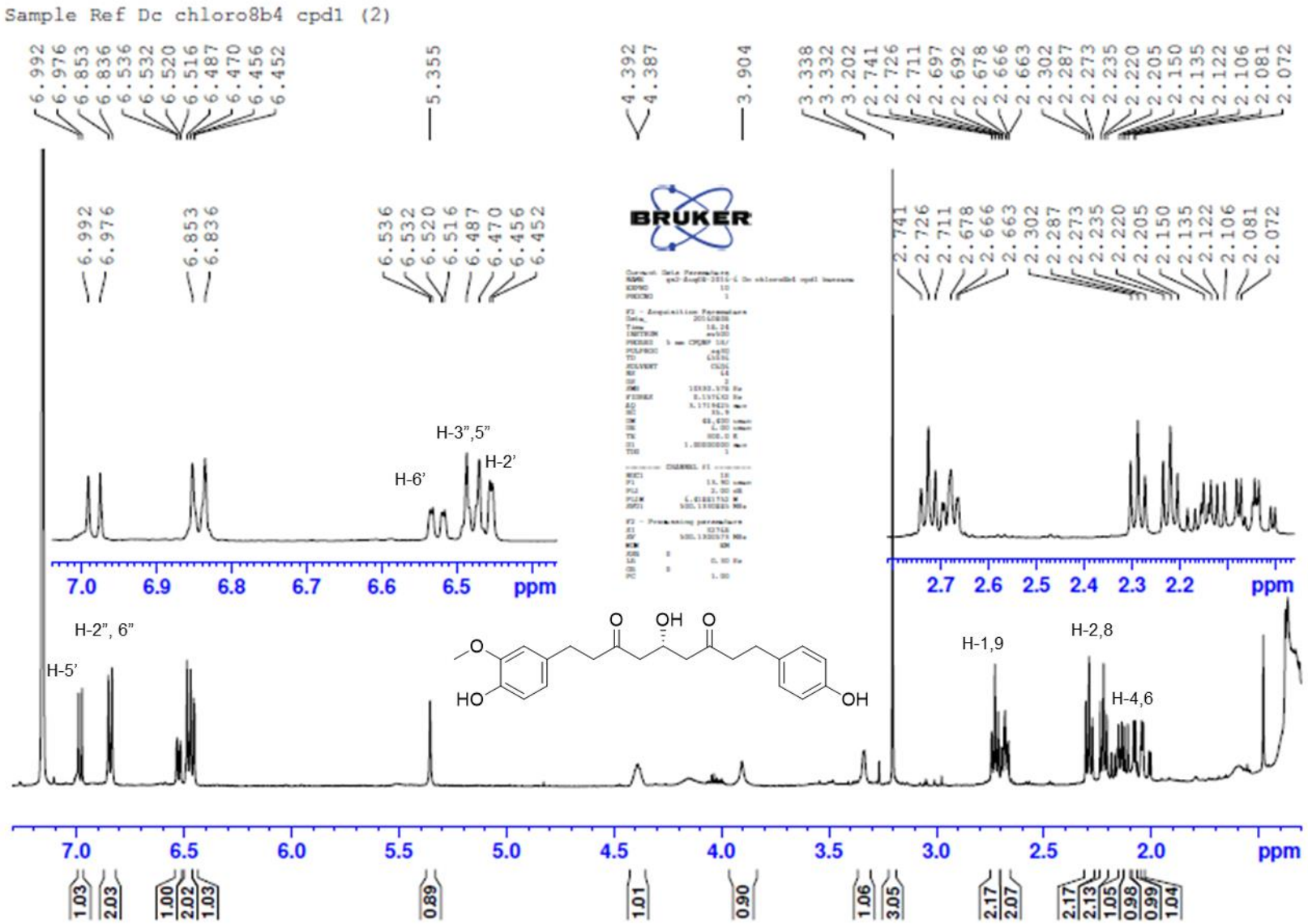

Figure S4: ^{1}H NMR spectrum of **1**, recorded in benzene-d_6, 500 MHz.

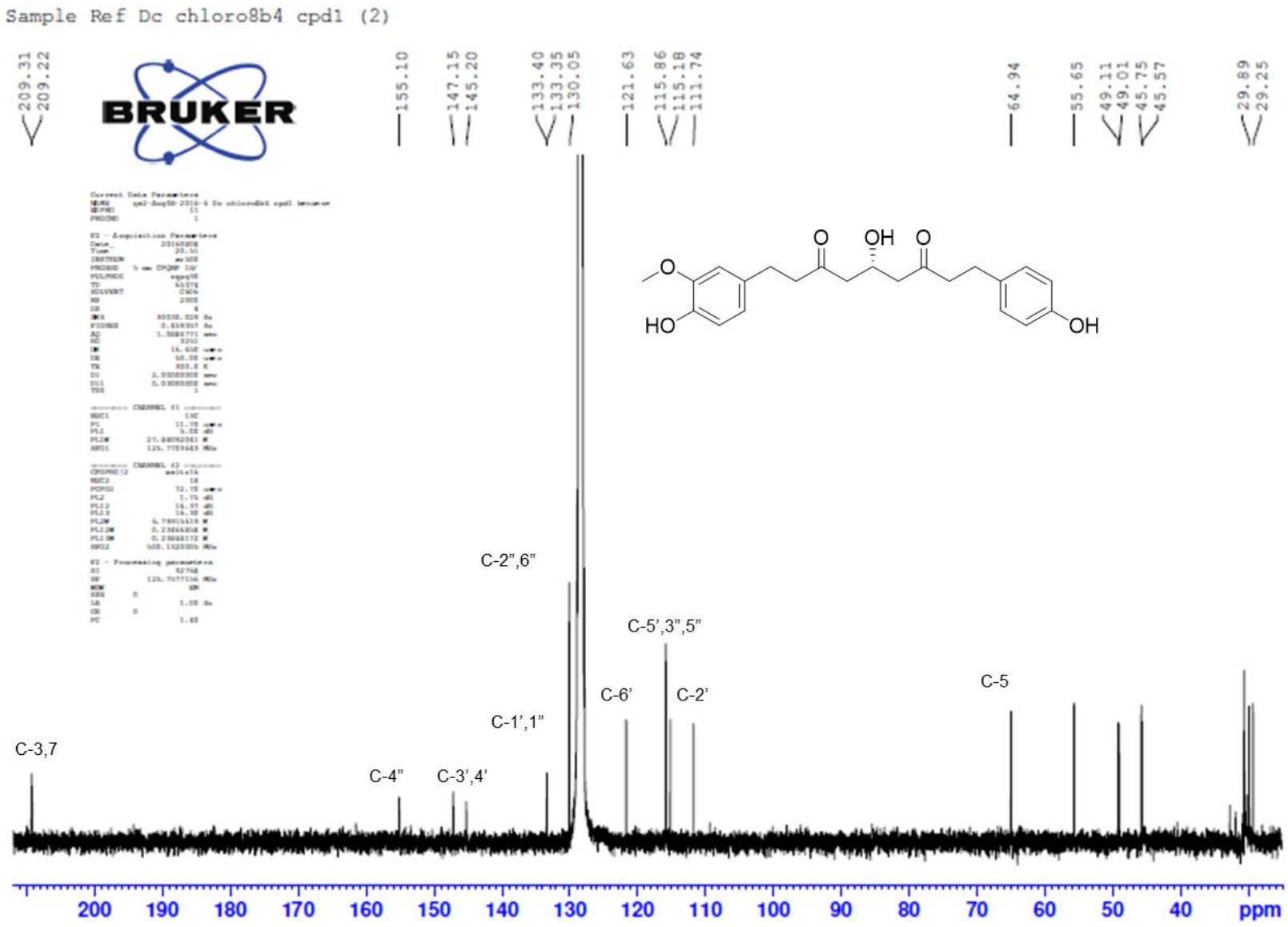

Figure S5: ^{13}C NMR spectrum of **1** recorded in benzene-d_6, 125 MHz.

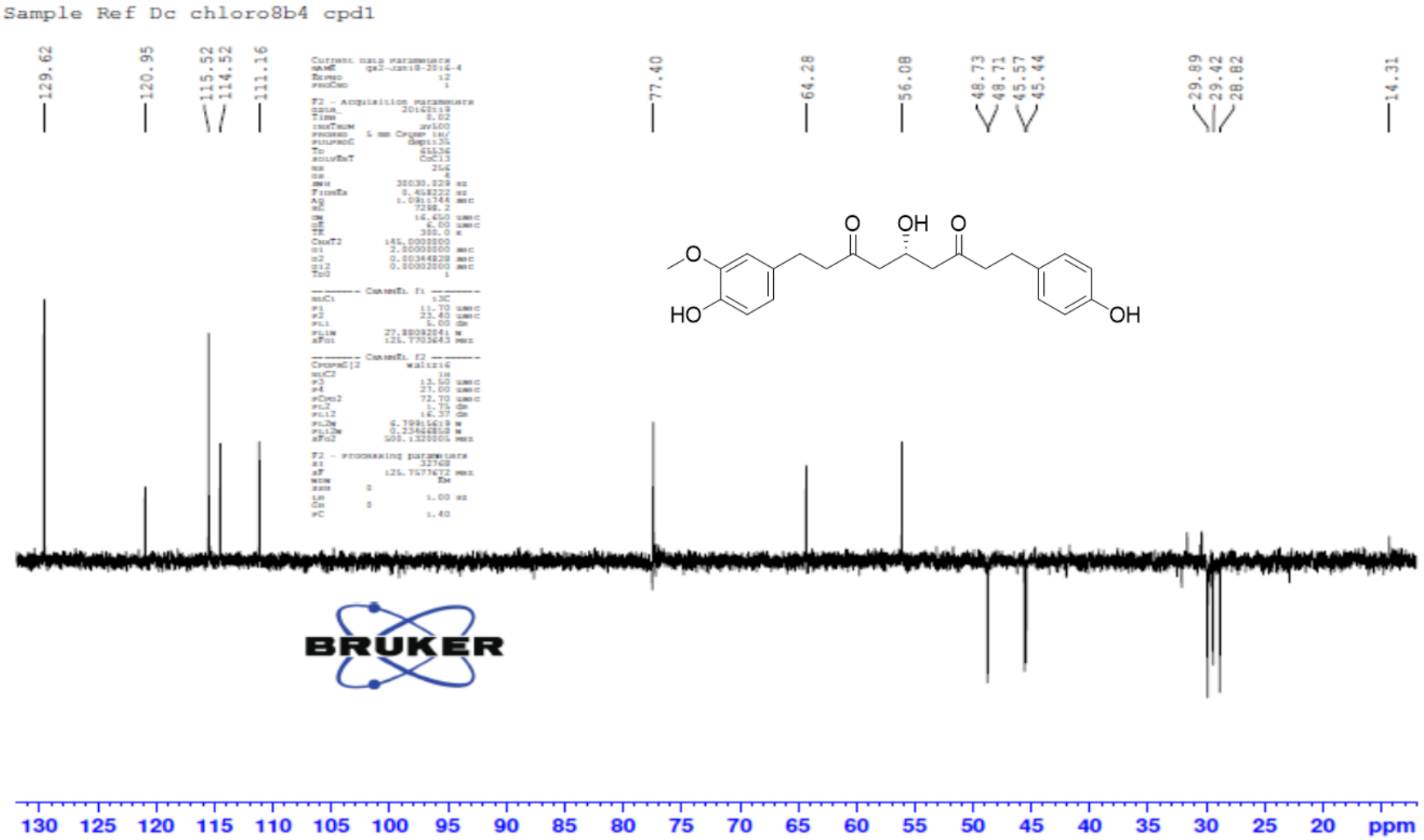

Figure S6: DEPT-135 spectrum of **1**, recorded in benzene-d_6, 125 MHz.

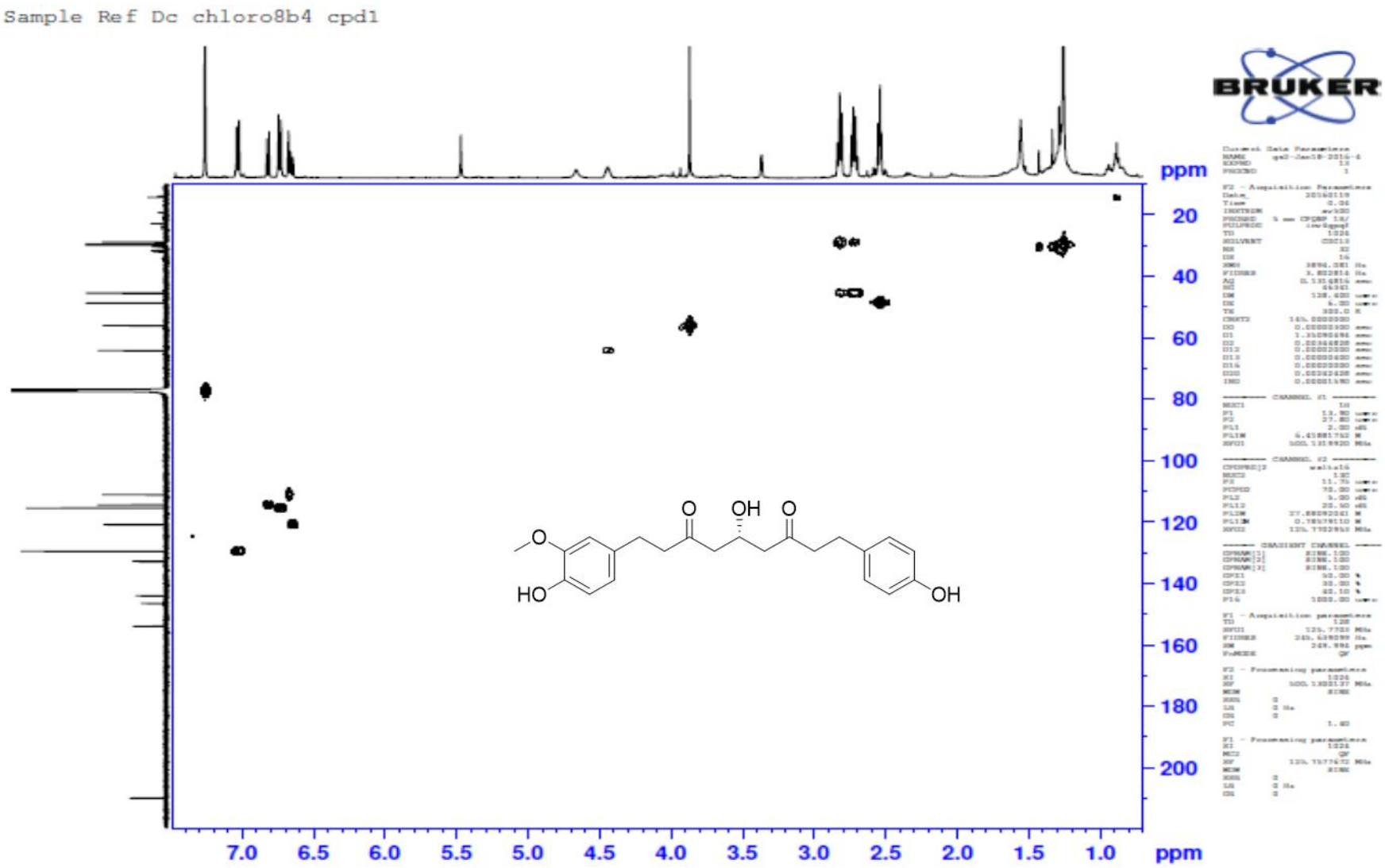

Figure S7: HMQC spectrum of **1**, recorded in benzene-d_6.

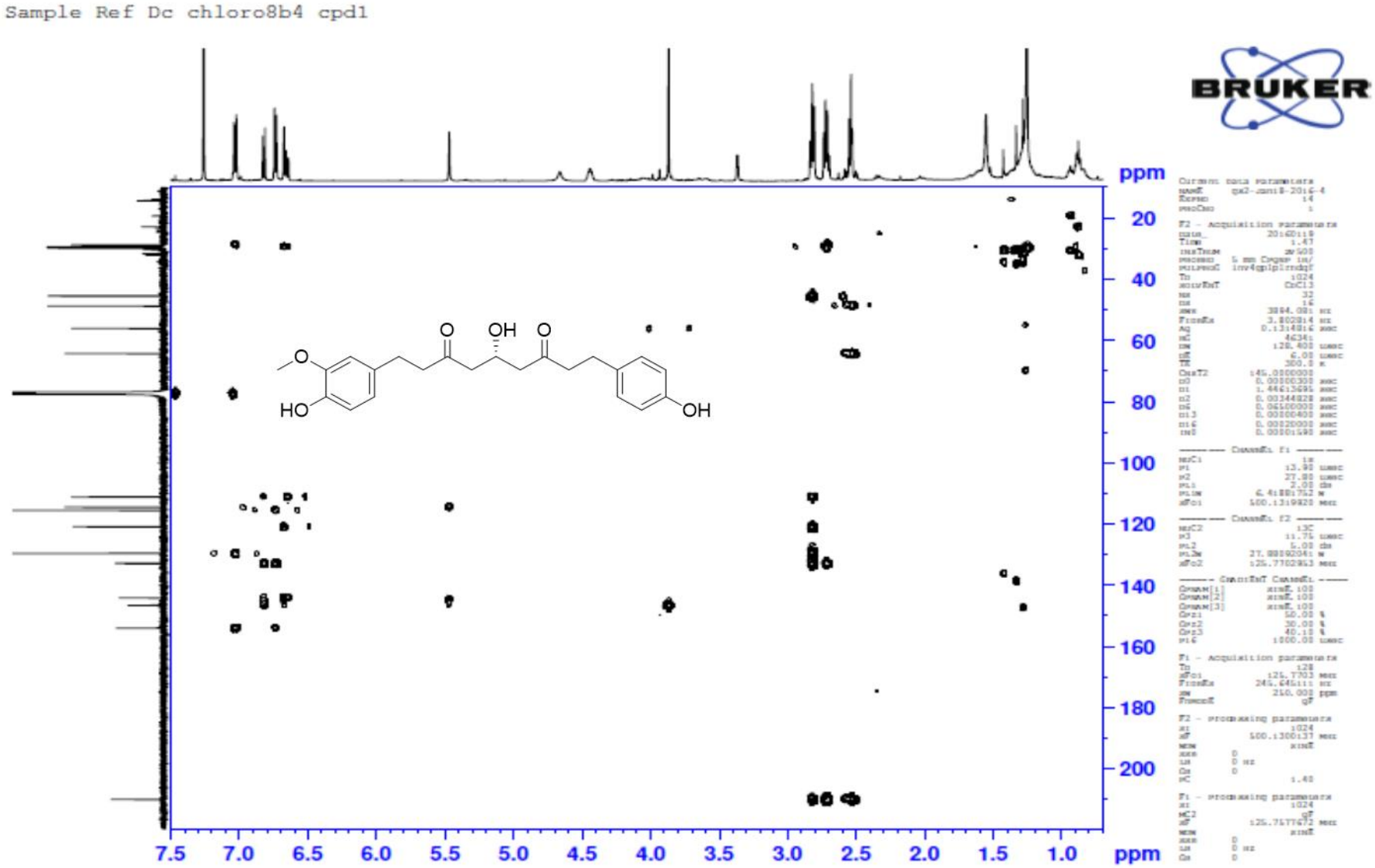

Figure S8: HMBC spectrum of **1**, recorded in benzene-d_6.

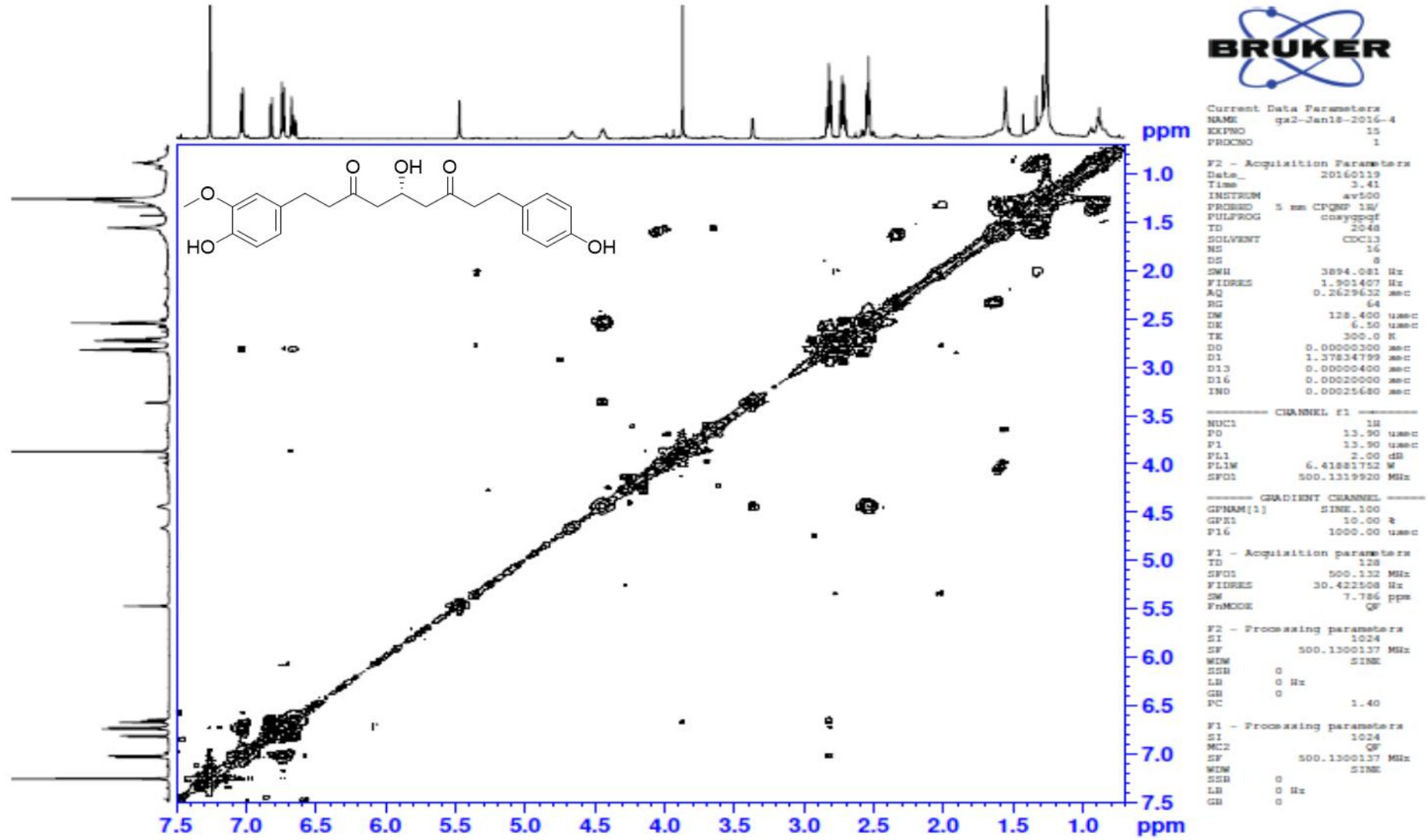

Figure S9: COSY spectrum of **1**, recorded in benzene-d_6.

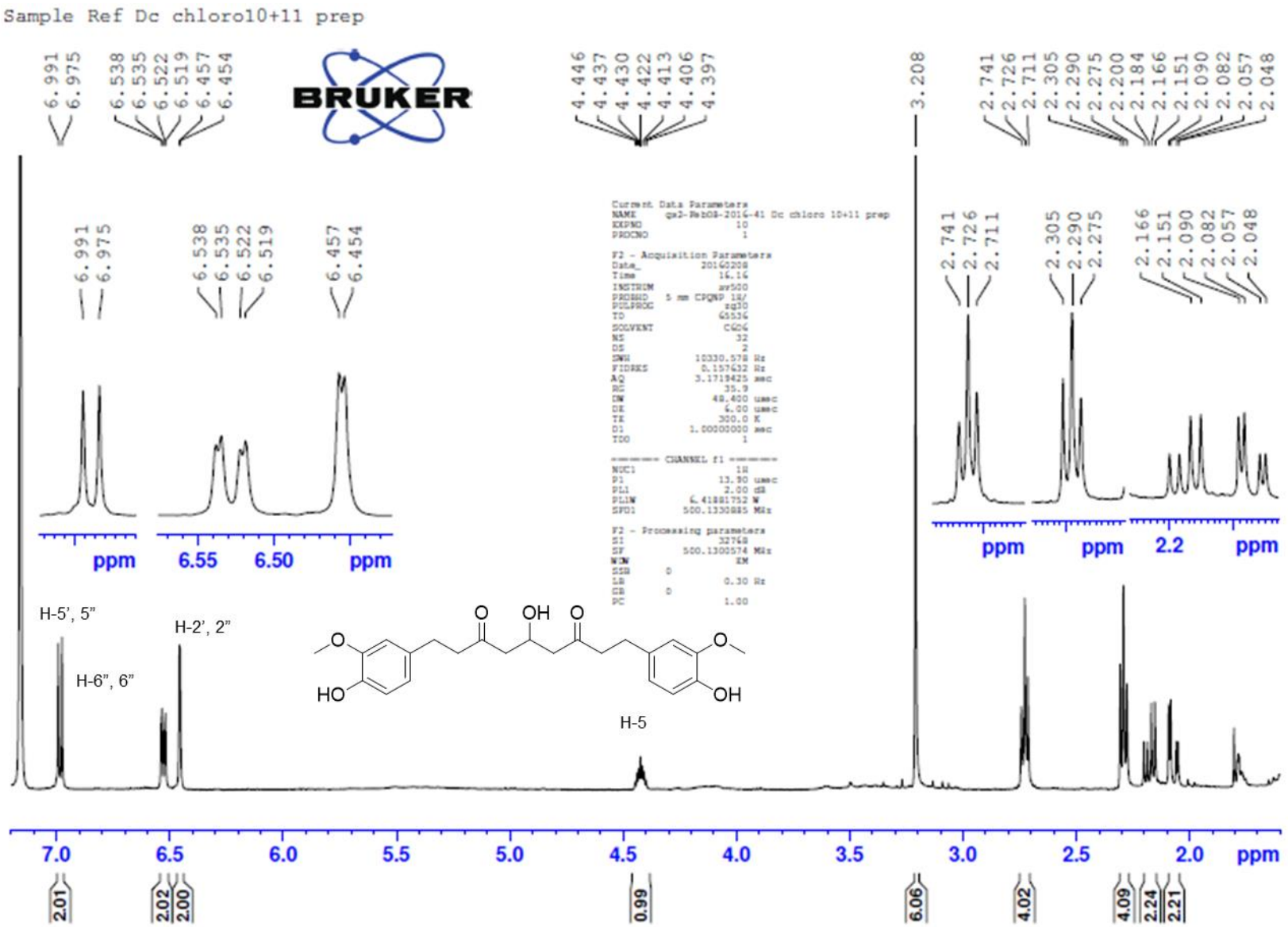

Figure S10: ^{1}H NMR spectrum of **2**, recorded in benzene-d_6, 500 MHz.

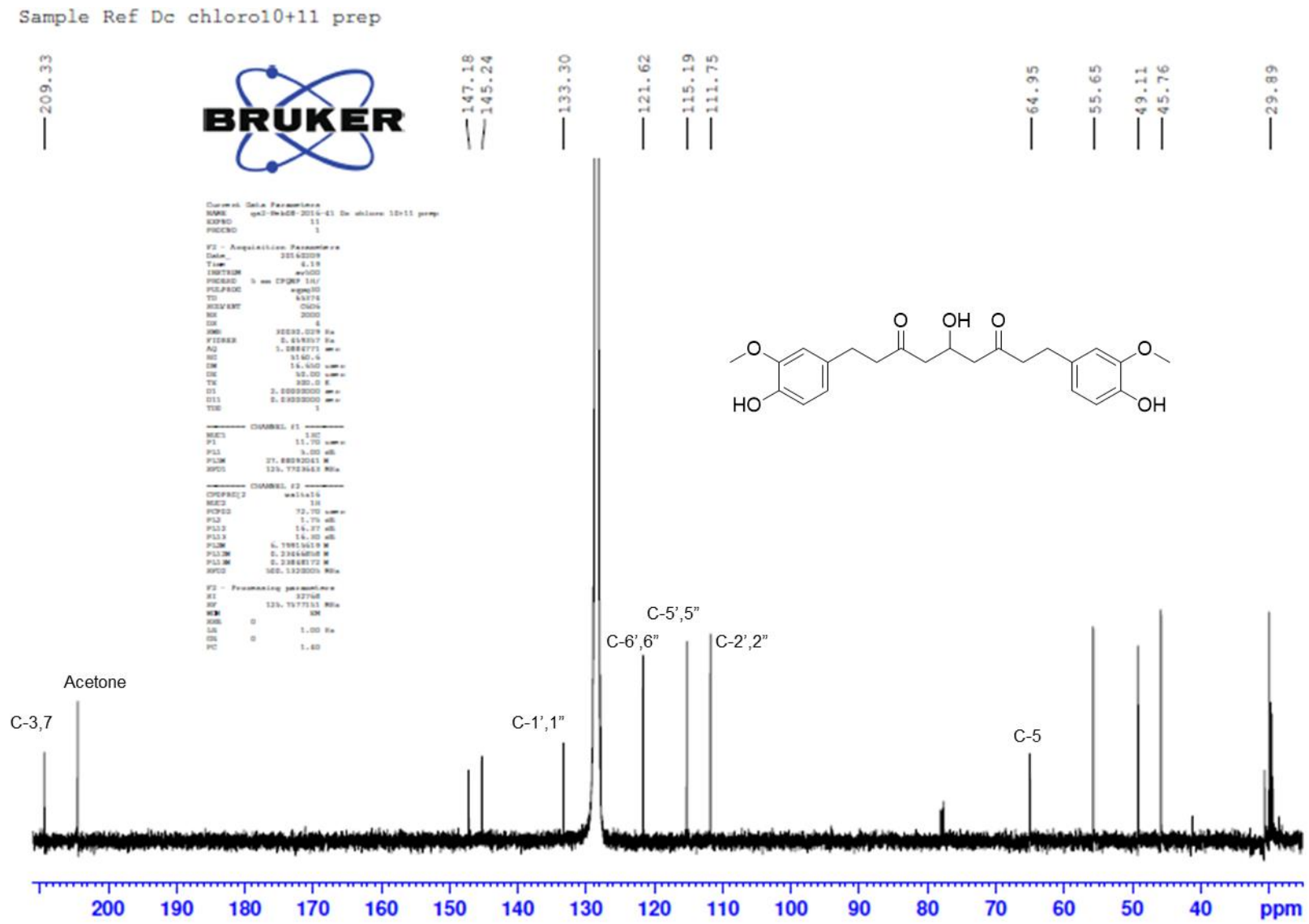

Figure S11: ^{13}C NMR spectrum of **2**, recorded in benzene-d_6, 125 MHz.

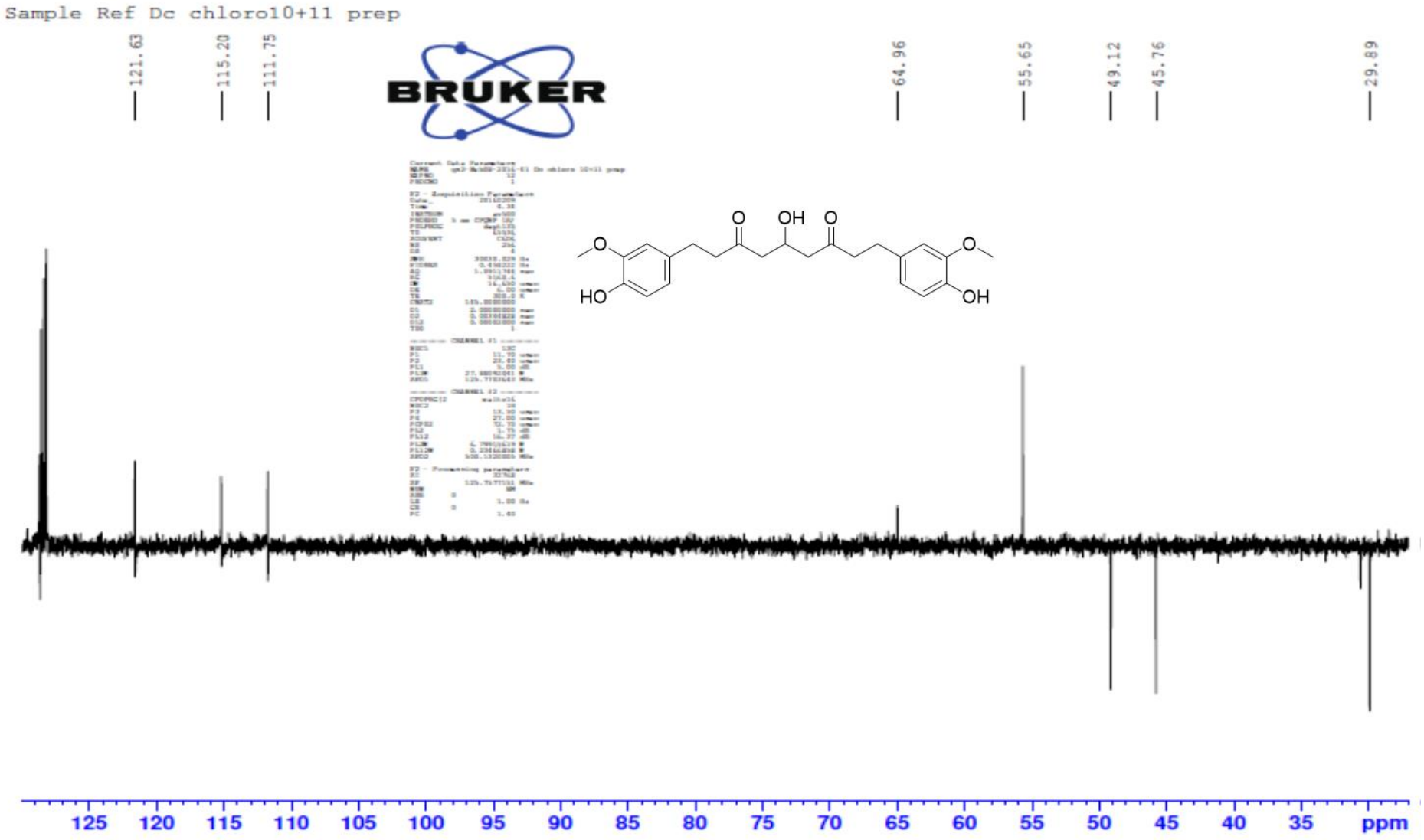

Figure S12: DEPT-135 spectrum of **2**, recorded in benzene-d_6, 125 MHz.

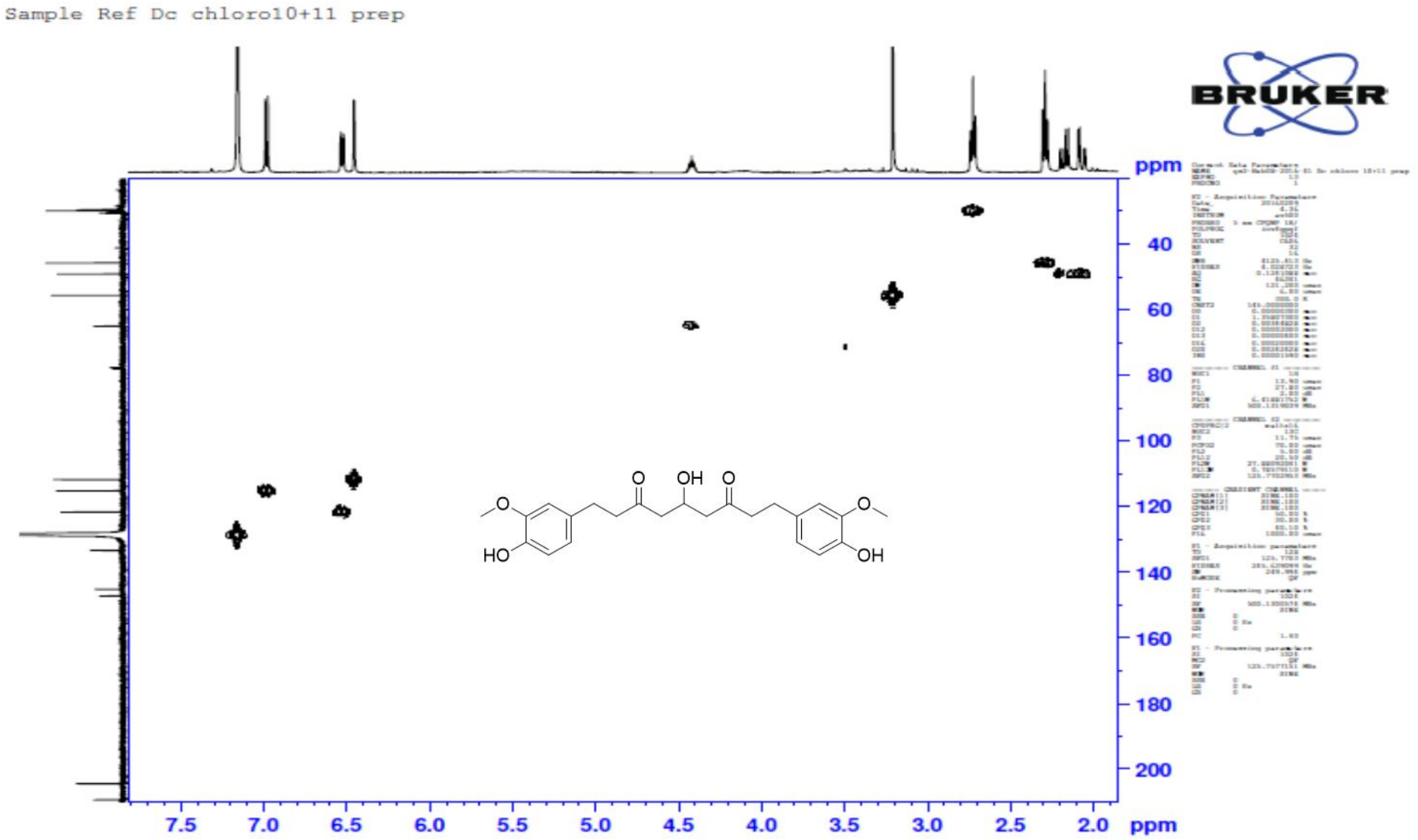

Figure S13: HMQC spectrum of **2**, recorded in benzene-d_6.

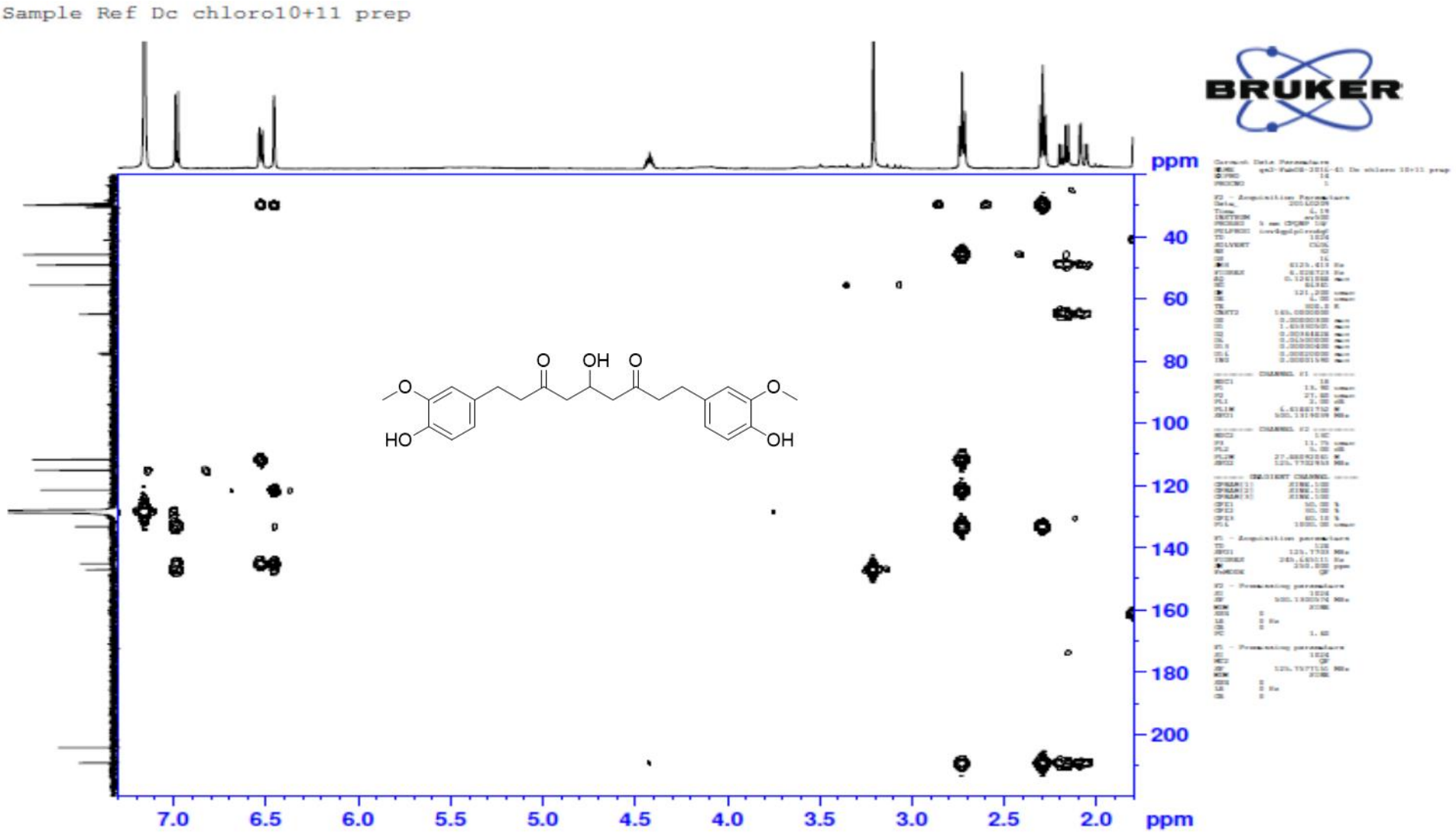

Figure S14: HMBC spectrum of **2**, recorded in benzene-d_6.

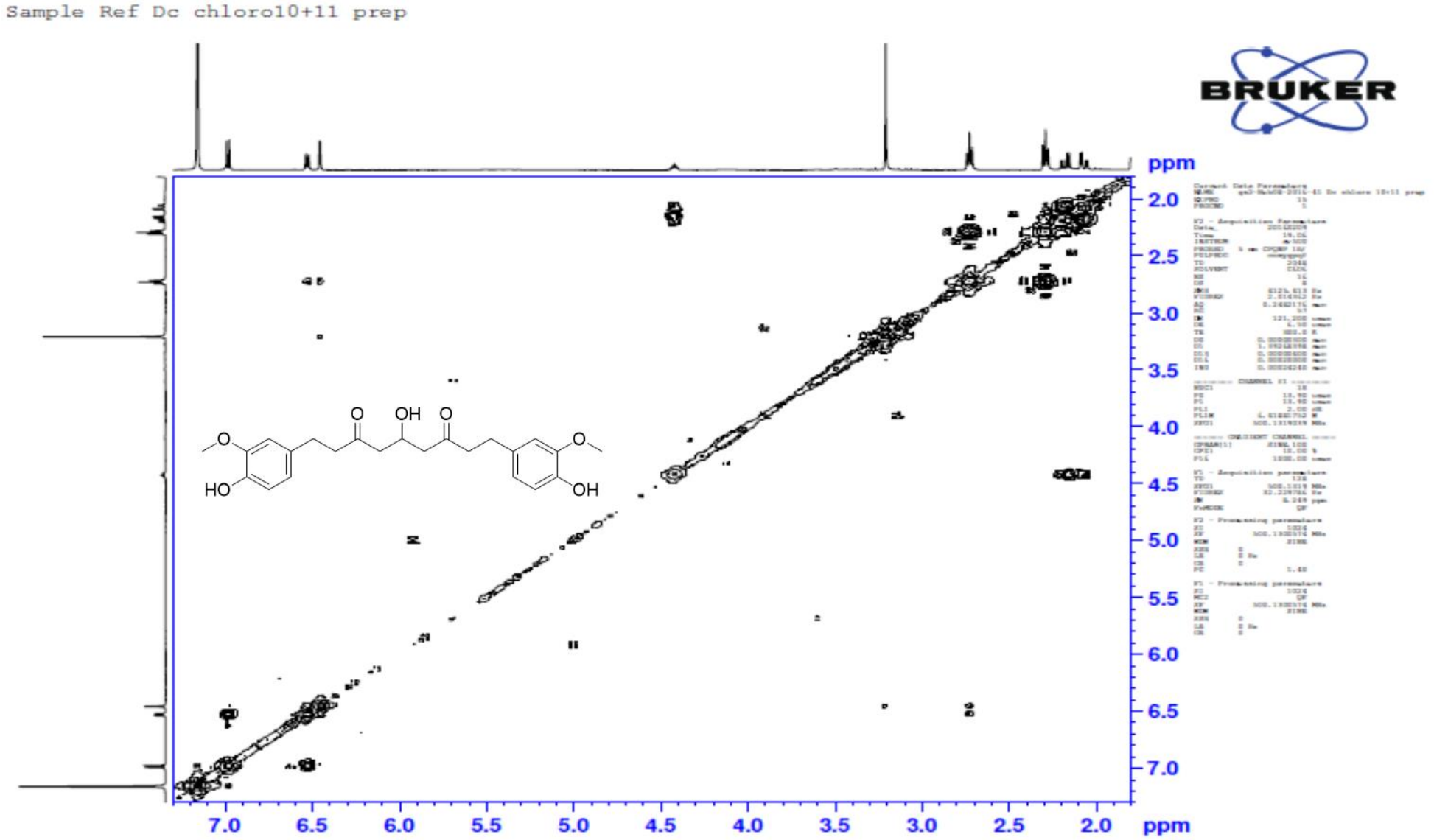

Figure S15: COSY spectrum of **2**, recorded in benzene-d_6.

Table **S**2: ^{1}H NMR data (500 MHz; multiplicities and coupling constants), ^{13}C NMR data (125 MHz) and HMBC correlations of **3**, recorded in $CDCl_3$.

no.	^{1}H	^{13}C	^{2}J	^{3}J
1 (2H)	4.19 (t, *J* = 6.5)	64.8	C-9’	C-3
2 – 3 (4H)	1.71 – 1.60 (m) overlapped	29.9 – 28.9		C-1
4 (2H)	1.41 – 1.25 (m) overlapped)	26.2		
5 – 27 (46H)	1.41 – 1.25 (m) overlapped)	29.9 – 28.9		C-4, C-28
28 – 29 (4H)	1.71 – 1.60 (m) overlapped	24.9	C-30	C-32
30 – 31 (4H)	2.34 (t, *J* = 7.5)	33.9	C-32	C-28
32		178.4		
1’		127.4		
2’	7.04 (d, *J* = 2.0)	109.5	C-1’, C-3’	C-7’, C-4’, C-6’, C-5’
3’		148.1		
4’		146.9		
5’	6.92 (d, *J* = 8.3)	114.9	C-6’, C-4’	C-1’
6’	7.07 (dd, *J* = 8.3, 2.0)	123.2	C-5’	C-2’, C-7’
7’	7.62 (d, *J* = 15.8)	144.8	C8’	C-2’, C-6’, C-9’
8’	6.31 (d, *J* = 15.8)	115.9	C9’, C-7’	C-1’
9’		167.6		
O$\underline{C}H_3$ – 4’	3.93 (s)	56.1	C-4’	

[chemical shift in ppm; coupling constants (Hz); multiplicity of proton signals: s; singlet, d; doublet, t; triplet, m; multiplet, dd; doublet of doublets]

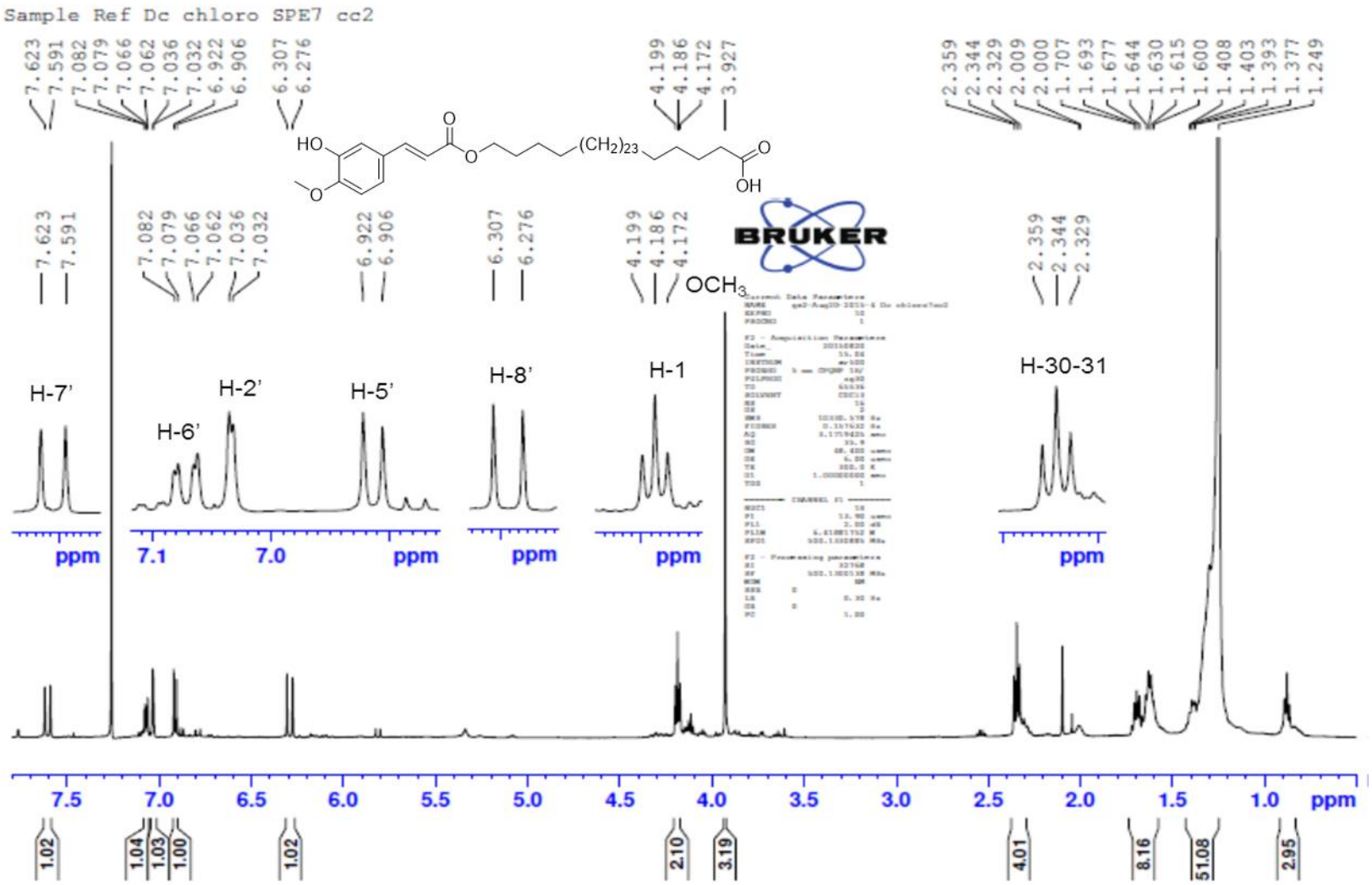

Figure S16: ^{1}H NMR spectrum of **3**, recorded in chloroform-*d*, 500 MHz.

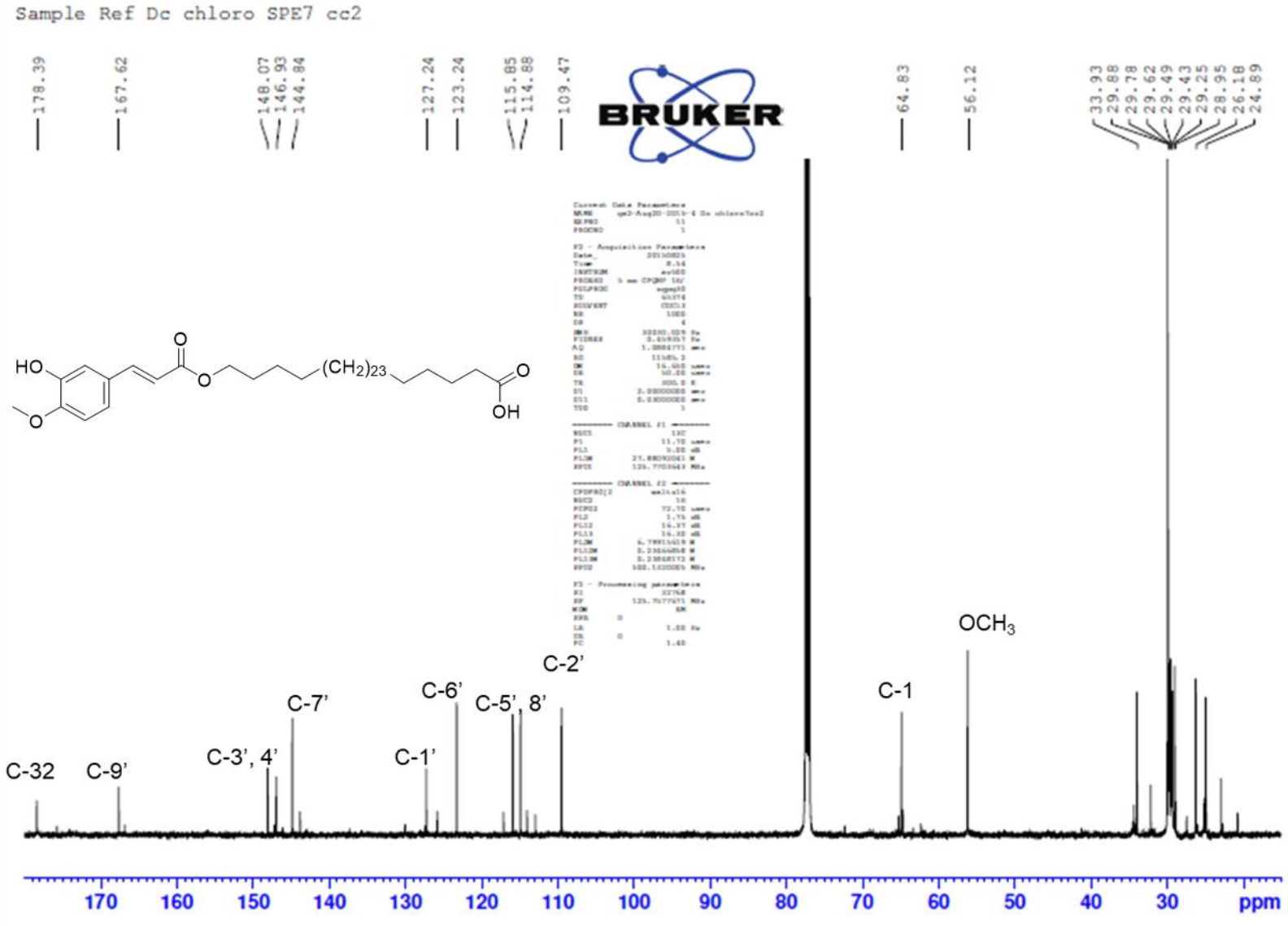

Figure S17: ^{13}C NMR spectrum of **3**, recorded in chloroform-d, 125 MHz.

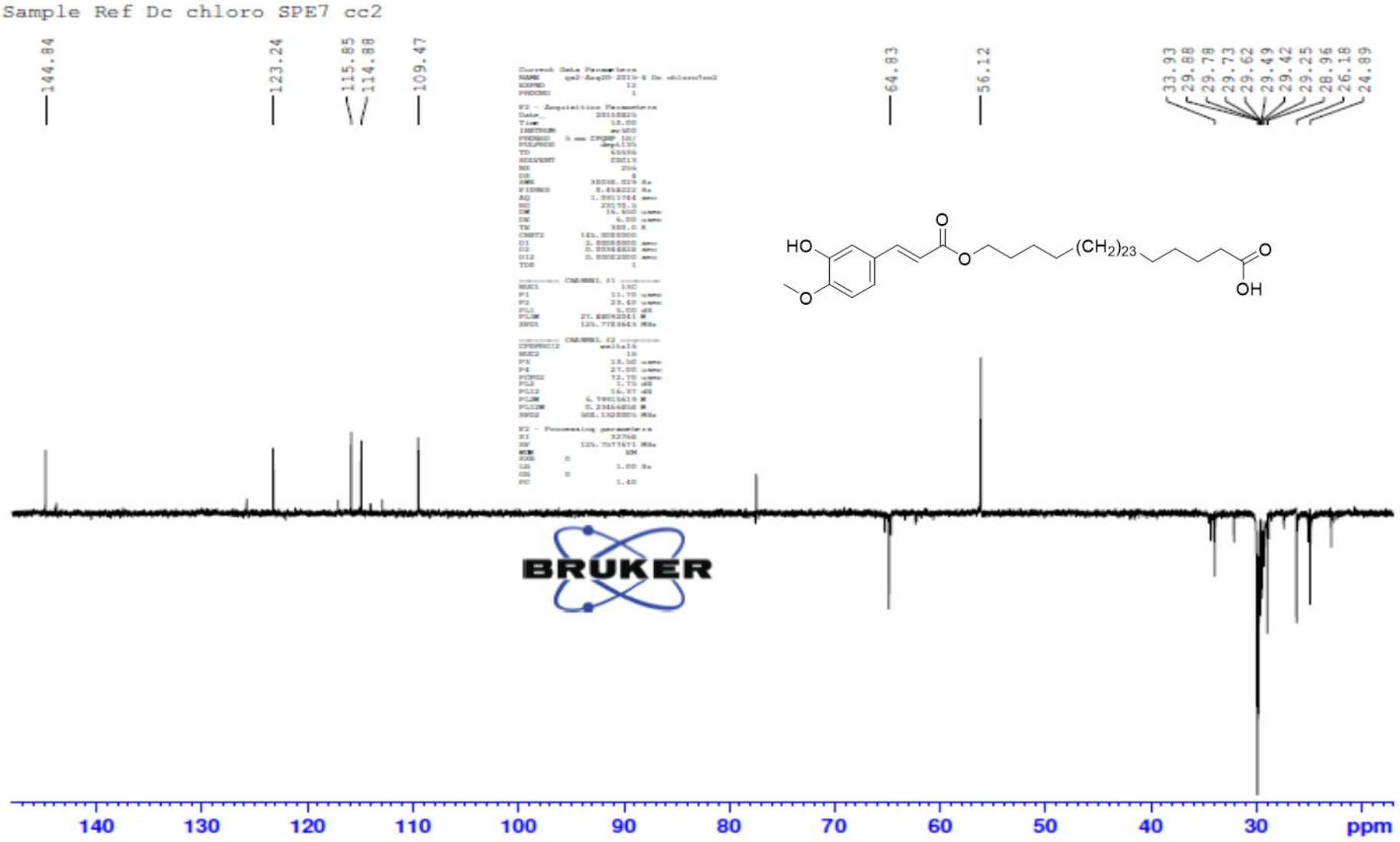

Figure S18: DEPT-135 spectrum of **3**, recorded in chloroform-*d*, 125 MHz.

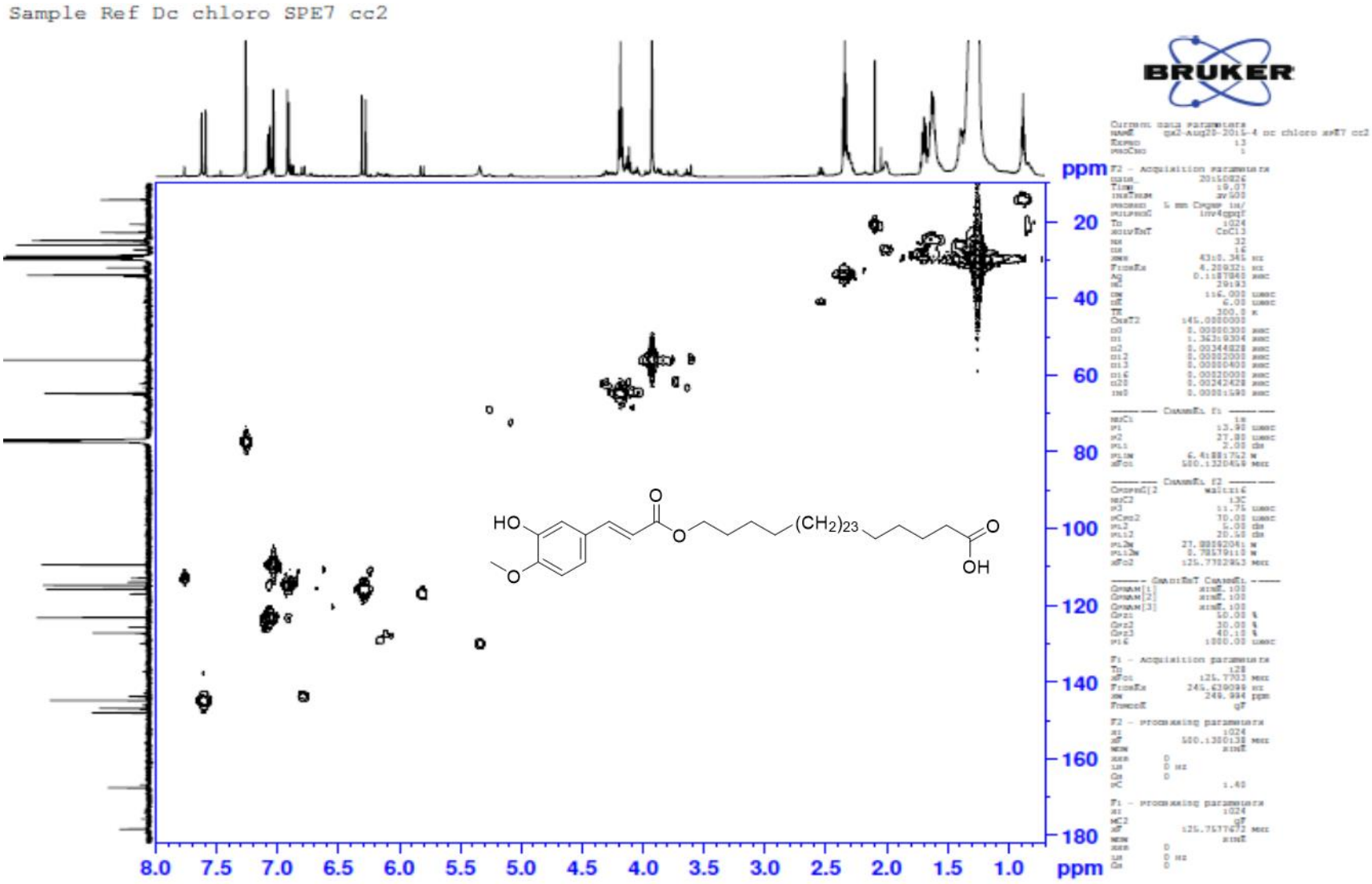

Figure S19: HMQC spectrum of **3**, recorded in chloroform-*d*.

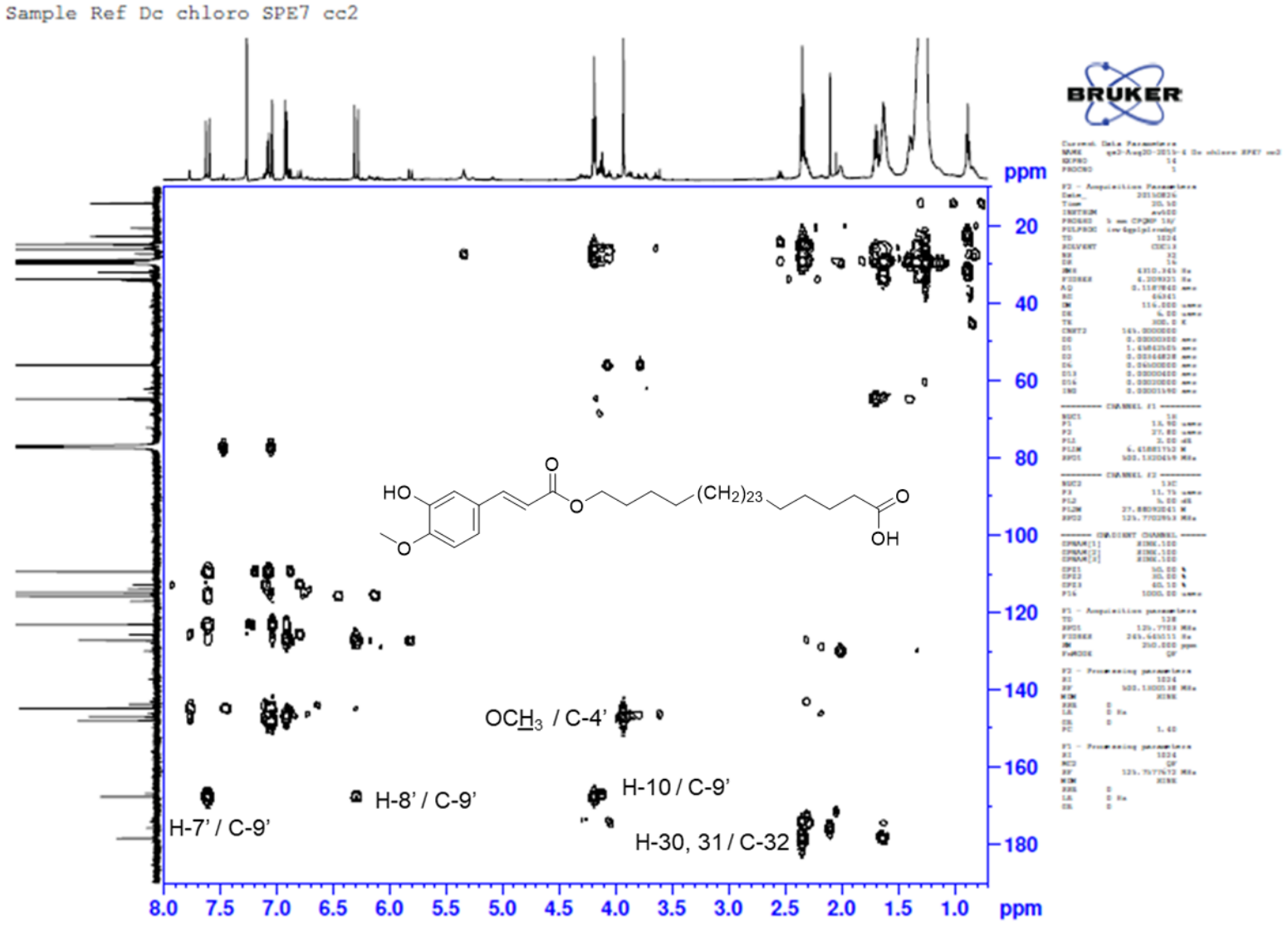

Figure S20: HMBC spectrum of **3**, recorded in chloroform-*d*.

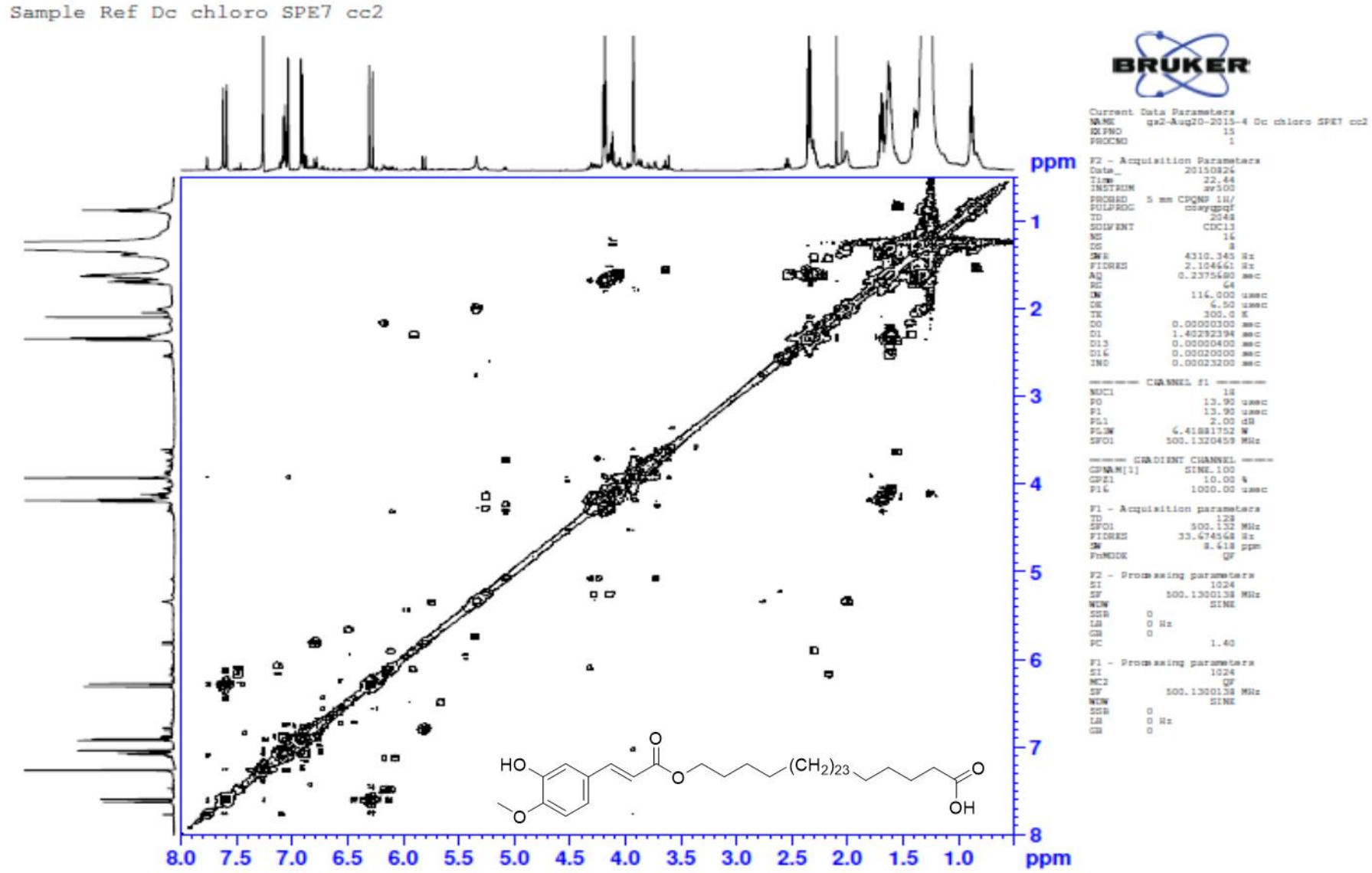

Figure S21: COSY spectrum of **3**, recorded in chloroform-*d*.

Table S3: ^{1}H NMR data (500 MHz; multiplicities and coupling constants), ^{13}C NMR data (125 MHz) and HMBC correlations of **4**, recorded in $CDCl_3$.

Position	^{1}H	^{13}C	^{2}J	^{3}J	^{13}C $CDCl_3$, 125 MHz
1		149.3			149.1
2		133.9			133.8
3		152.3			152.1
4	6.26 (d, *J* = 1.8)	104.6	C-3, C-5	C-6, C-7	104.5
5		138.5			138.2
6	6.50 (d, *J* = 1.8)	108.0	C-1	C-4	107.8
7	2.84, 2.90 (m)	36.5	C-5, C-8	C-6	36.8
8	2.80, 2.87 (m)	32.4	C1', C-2'	C-6'	32.2
1'		127.9			127.8
2'		153.7			153.5
3'	6.76 (d, *J* = 7.5)	115.5	C-2'		115.4
4'	6.86 (ddd, *J* = 7.5, 7.0, 1,0)	121.0		C-2'	120.9
5'	7.09 (dd, unresolved)	127.5	C-6'		127.3
6'	7.09 (d, *J* = 7.5), overlapped	130.5		C-2'	130.4
O<u>CH</u>$_3$ – 2	3.87 (s)	61.2		C-2	61.0
O<u>CH</u>$_3$ – 3	3.80 (s)	56.0		C-3	55.8
O<u>H</u> – 1	5.73 (brd)				
O<u>H</u> – 2'	4.72 (brd)				

[chemical shift in ppm; coupling constants (Hz); multiplicity of proton signals: s; singlet, d; doublet, m; multiplet, brd; broad; dd; doublet of doublets]

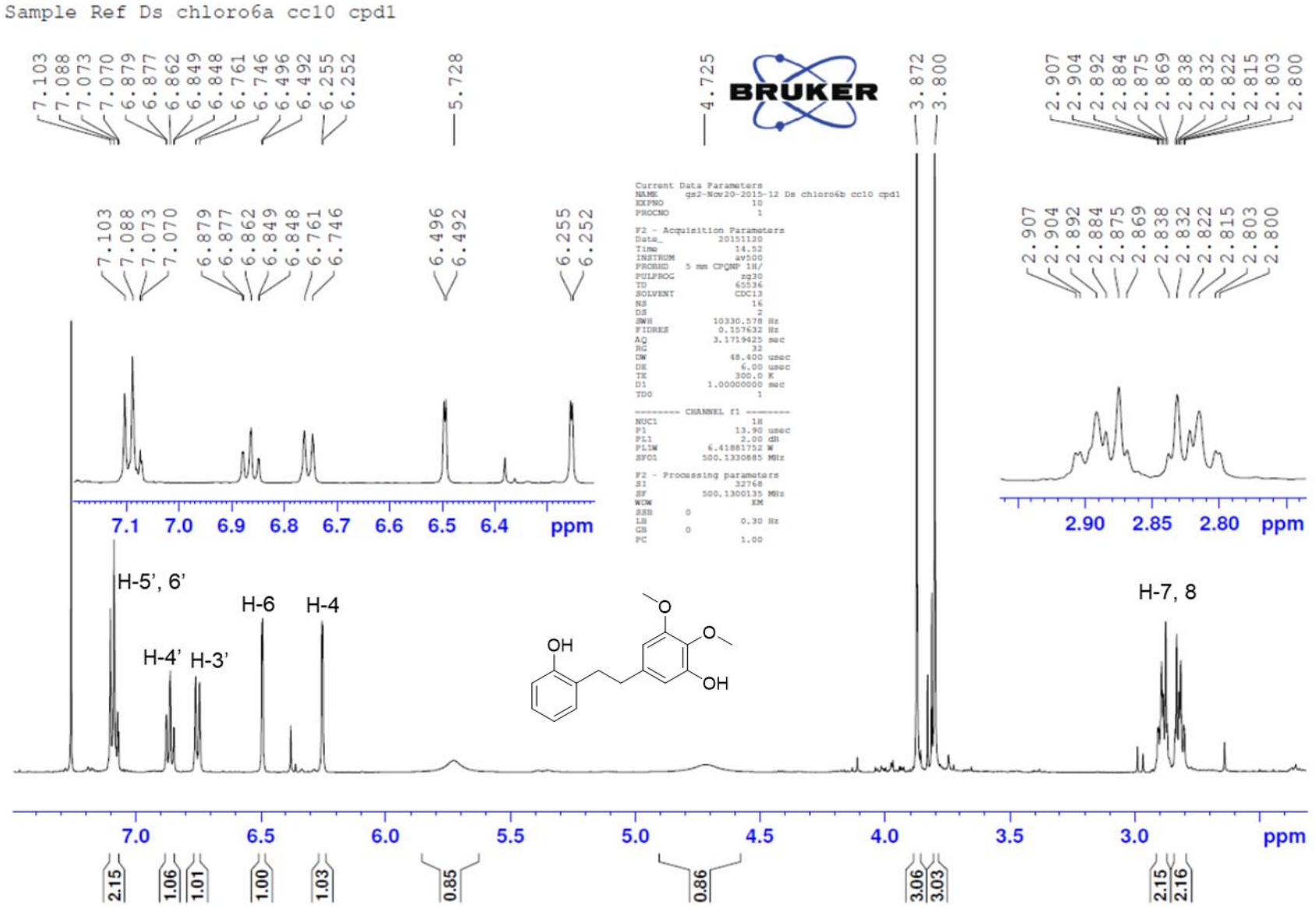

Figure S22: ^{1}H NMR spectrum of **4**, recorded in chloroform-*d*, 500 MHz.

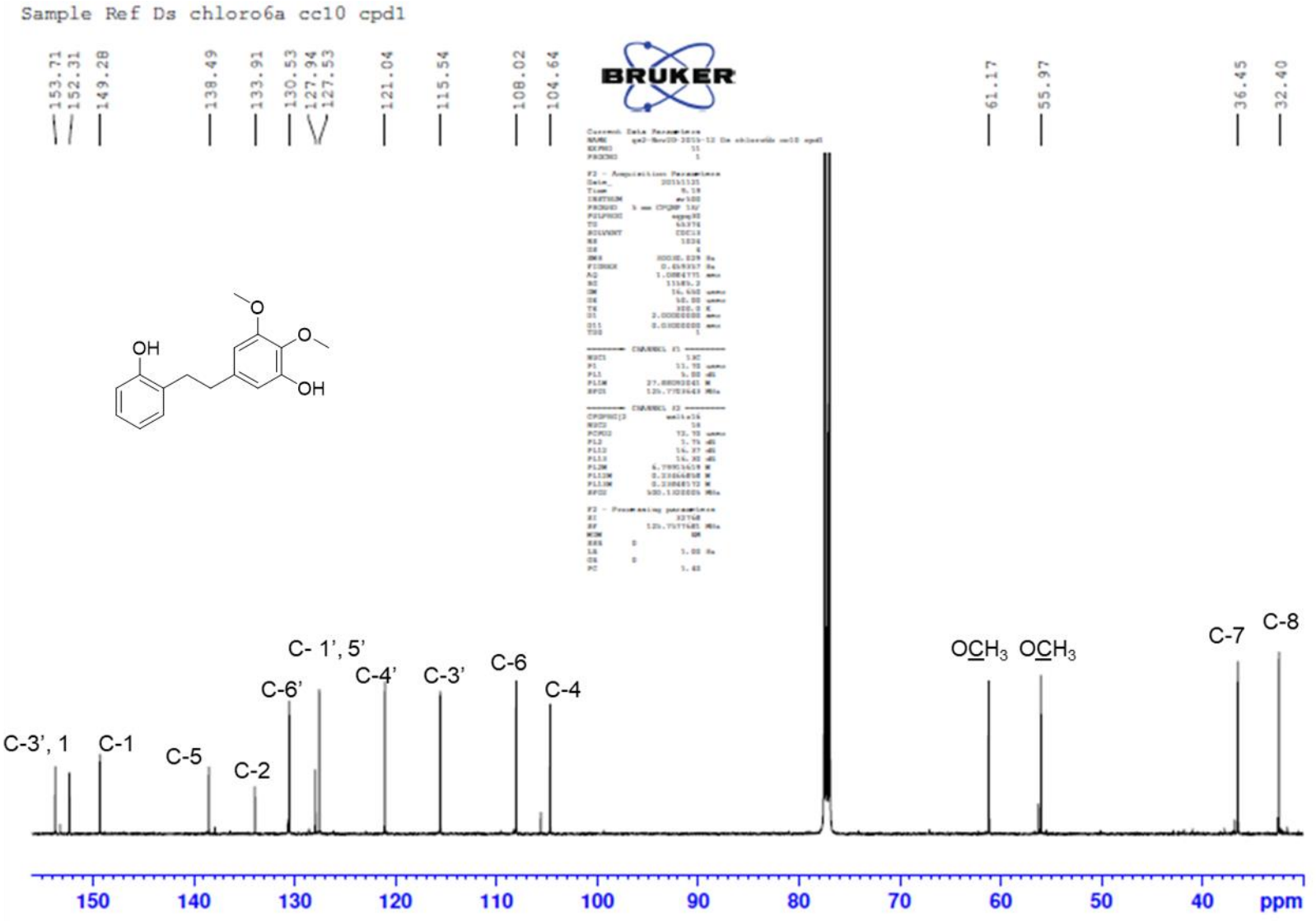

Figure S23: ^{13}C NMR spectrum of **4**, recorded in chloroform-*d*, 125 MHz.

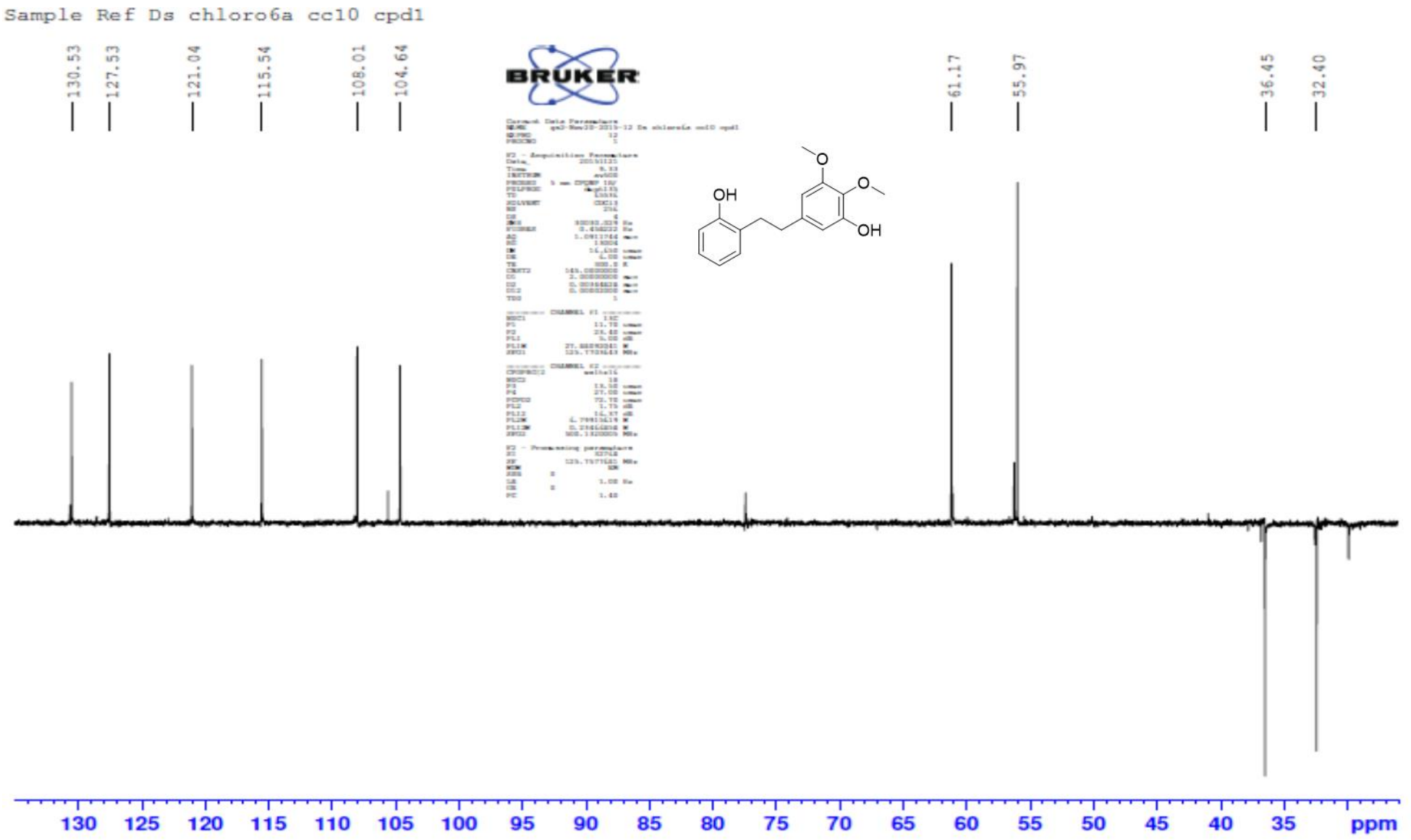

Figure S24: DEPT-135 spectrum of **4**, recorded in chloroform-*d*, 125 MHz.

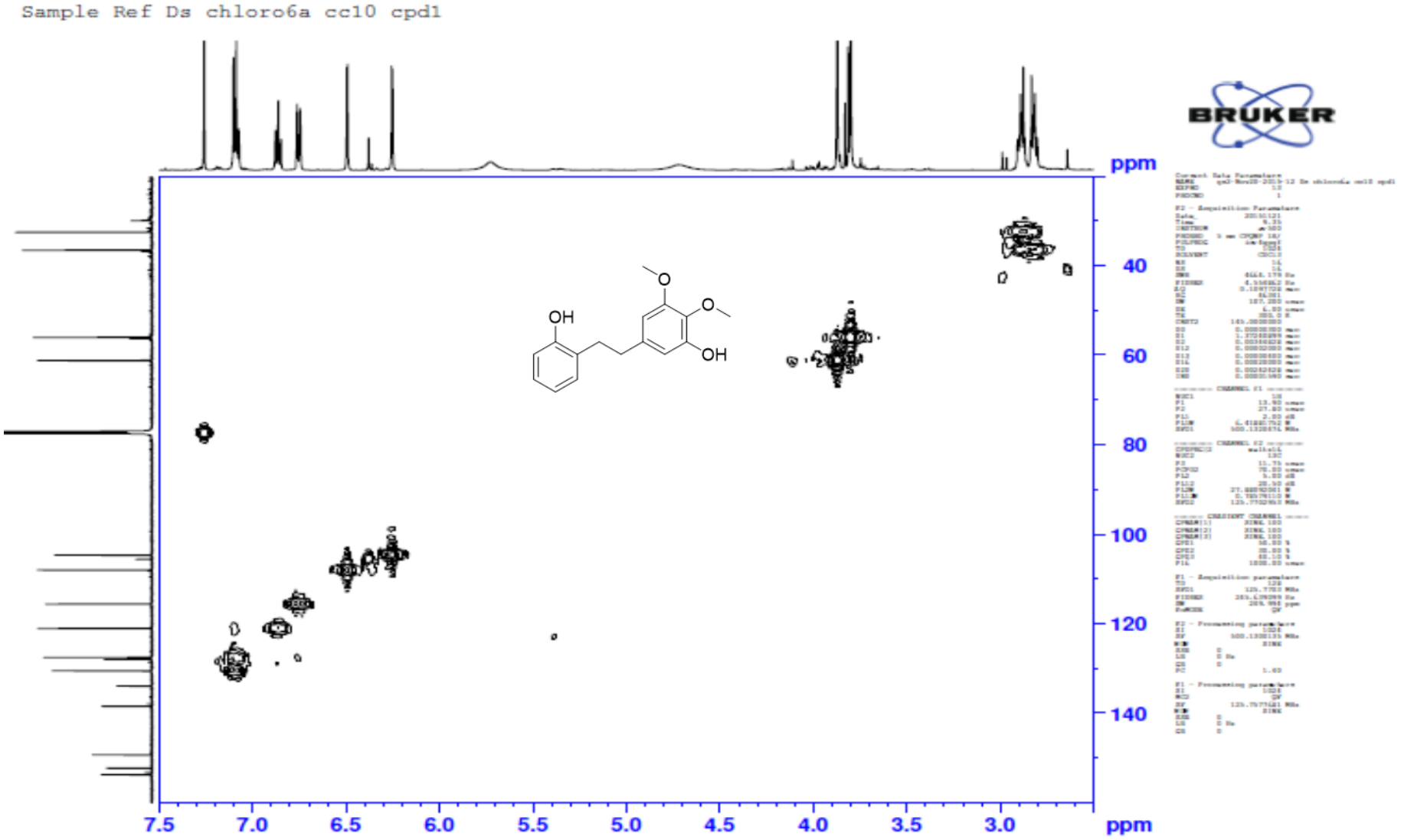

Figure S25: HMQC spectrum of **4**, recorded in chloroform-*d*.

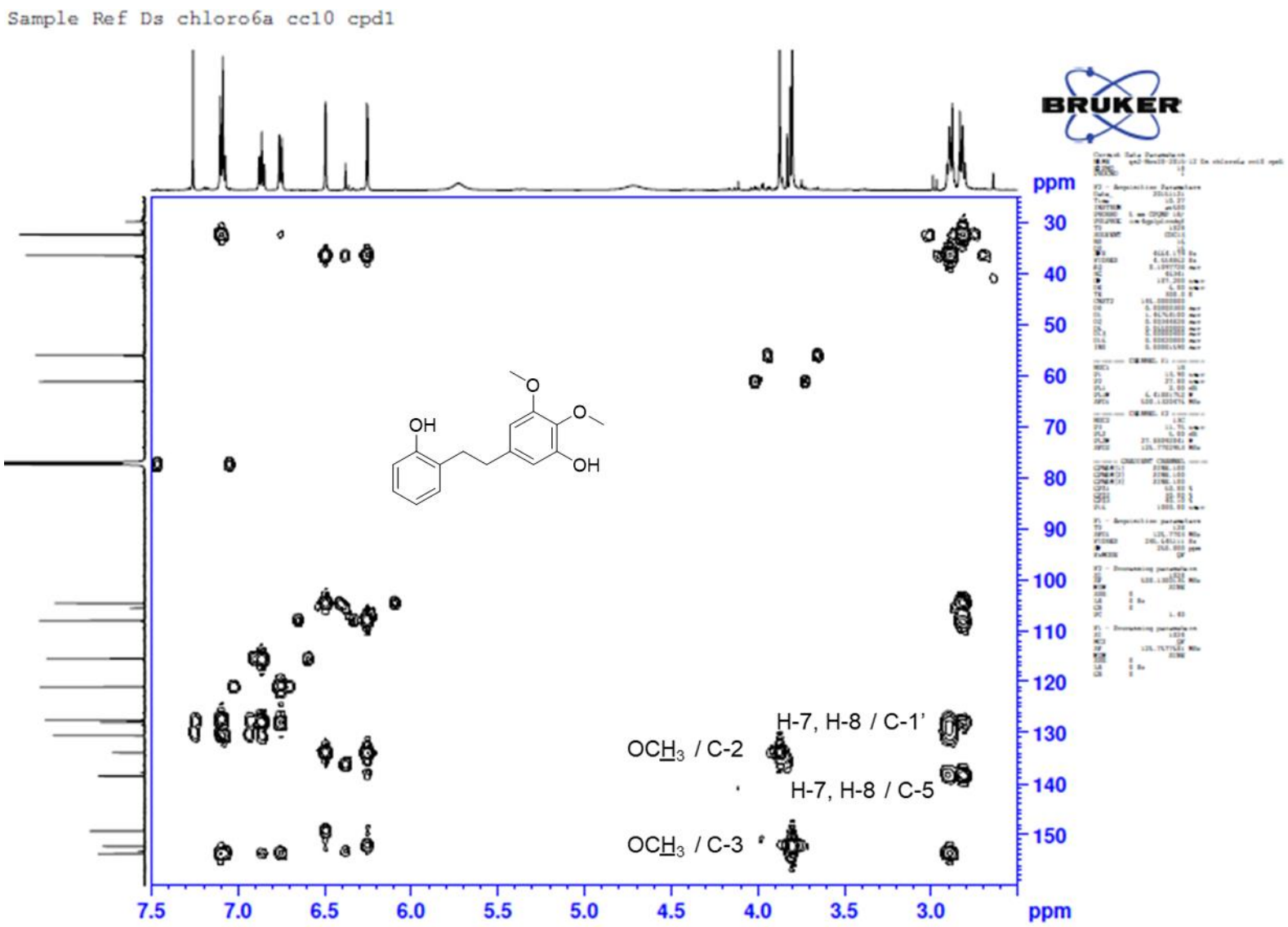

Figure S26: HMBC spectrum of **4**, recorded in chloroform-*d*.

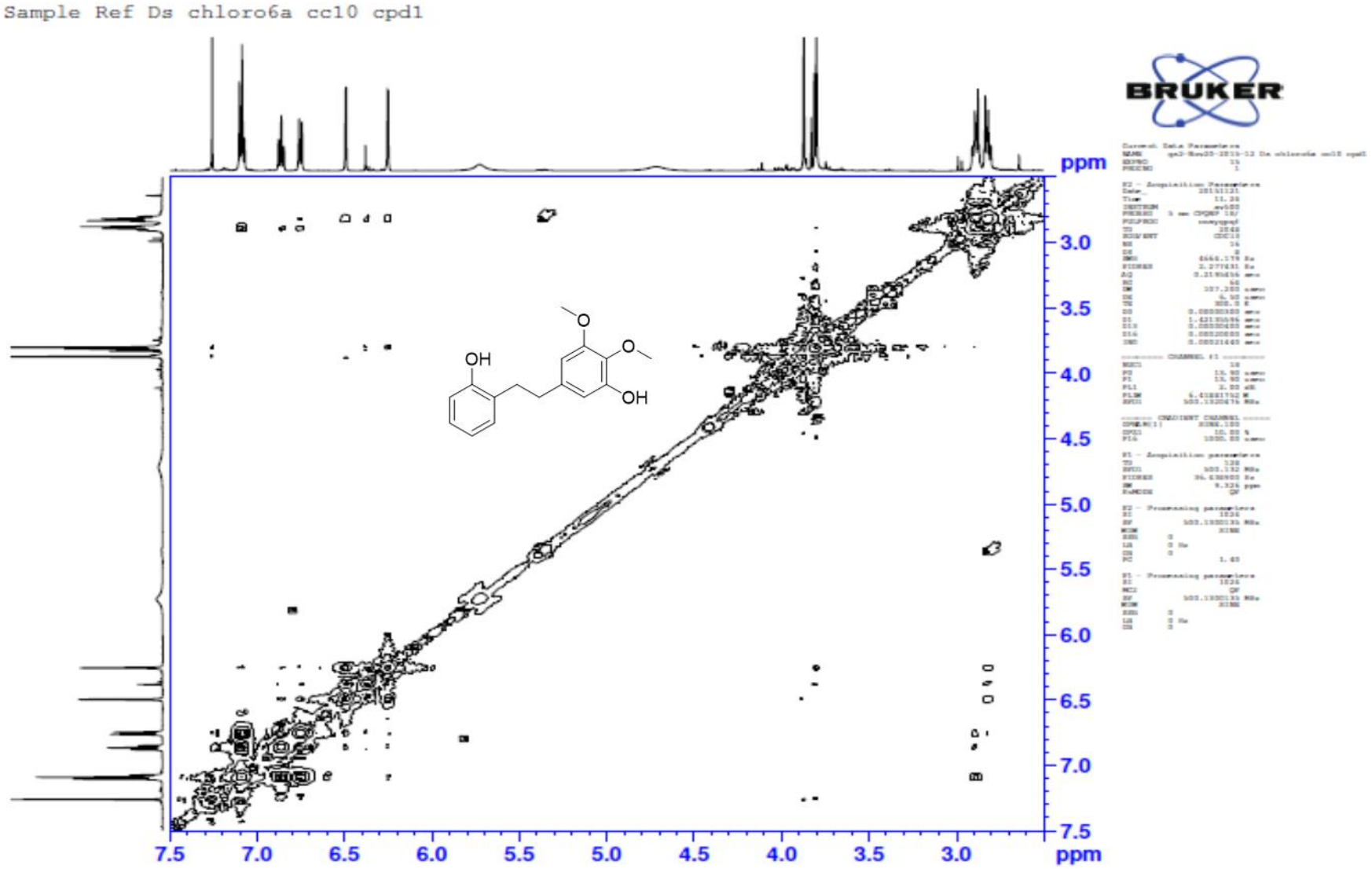

Figure S27: COSY spectrum of **4**, recorded in chloroform-*d*

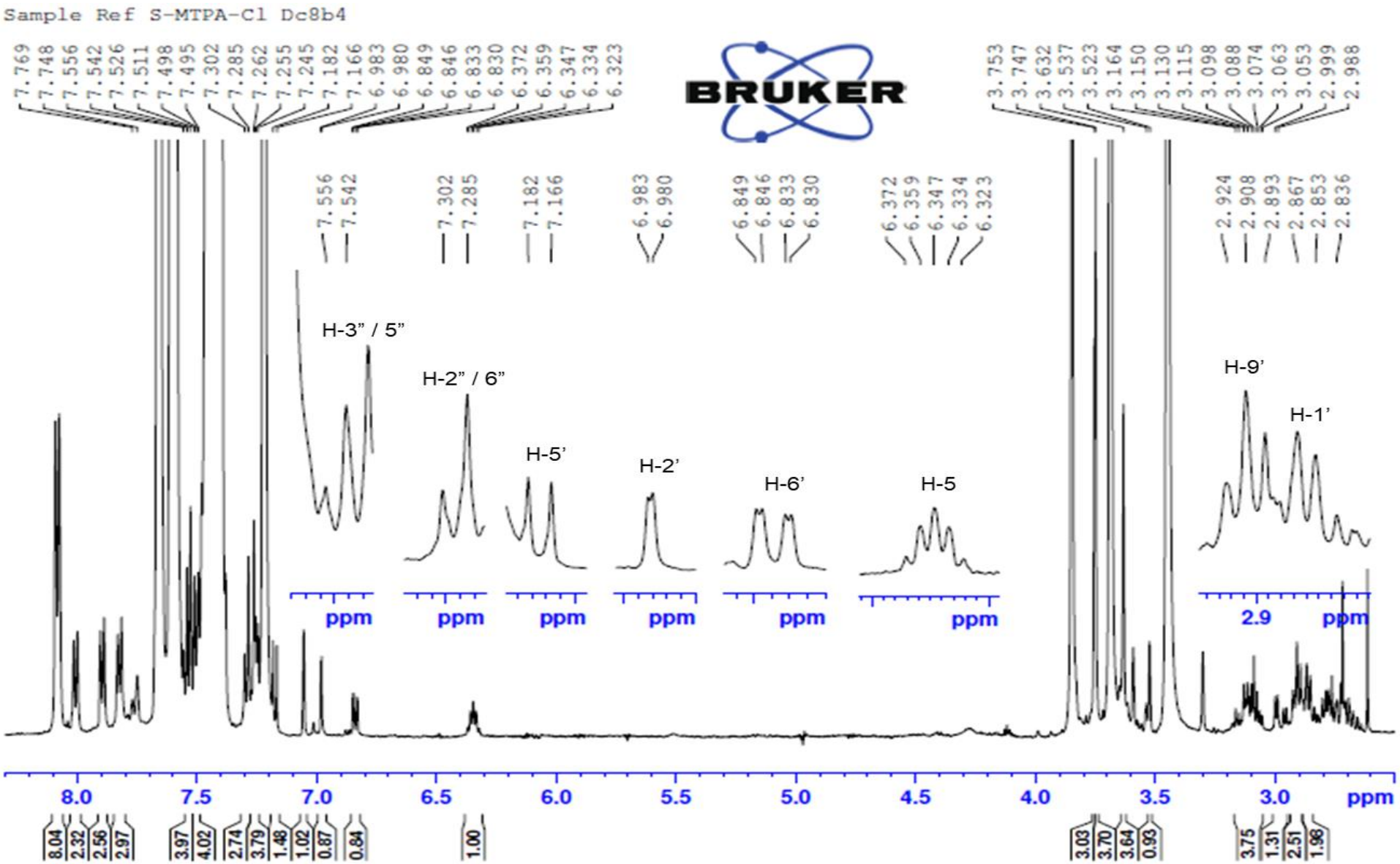

Figure S28: ^{1}H NMR spectrum of the (*R*)-MPTA ester of **1**.

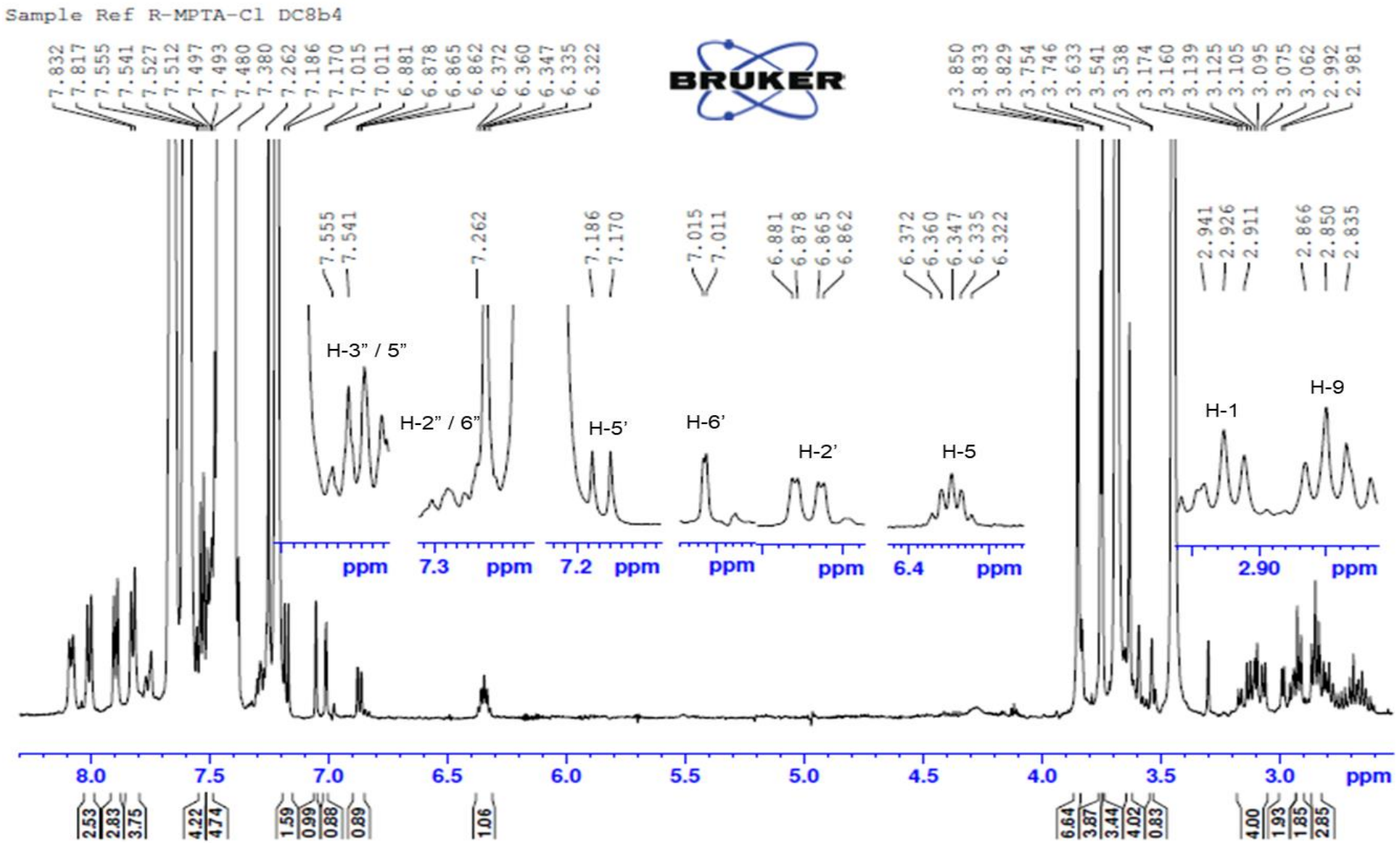

Figure S29: ^{1}H NMR spectrum of the (*S*)-MPTA ester of **1.**